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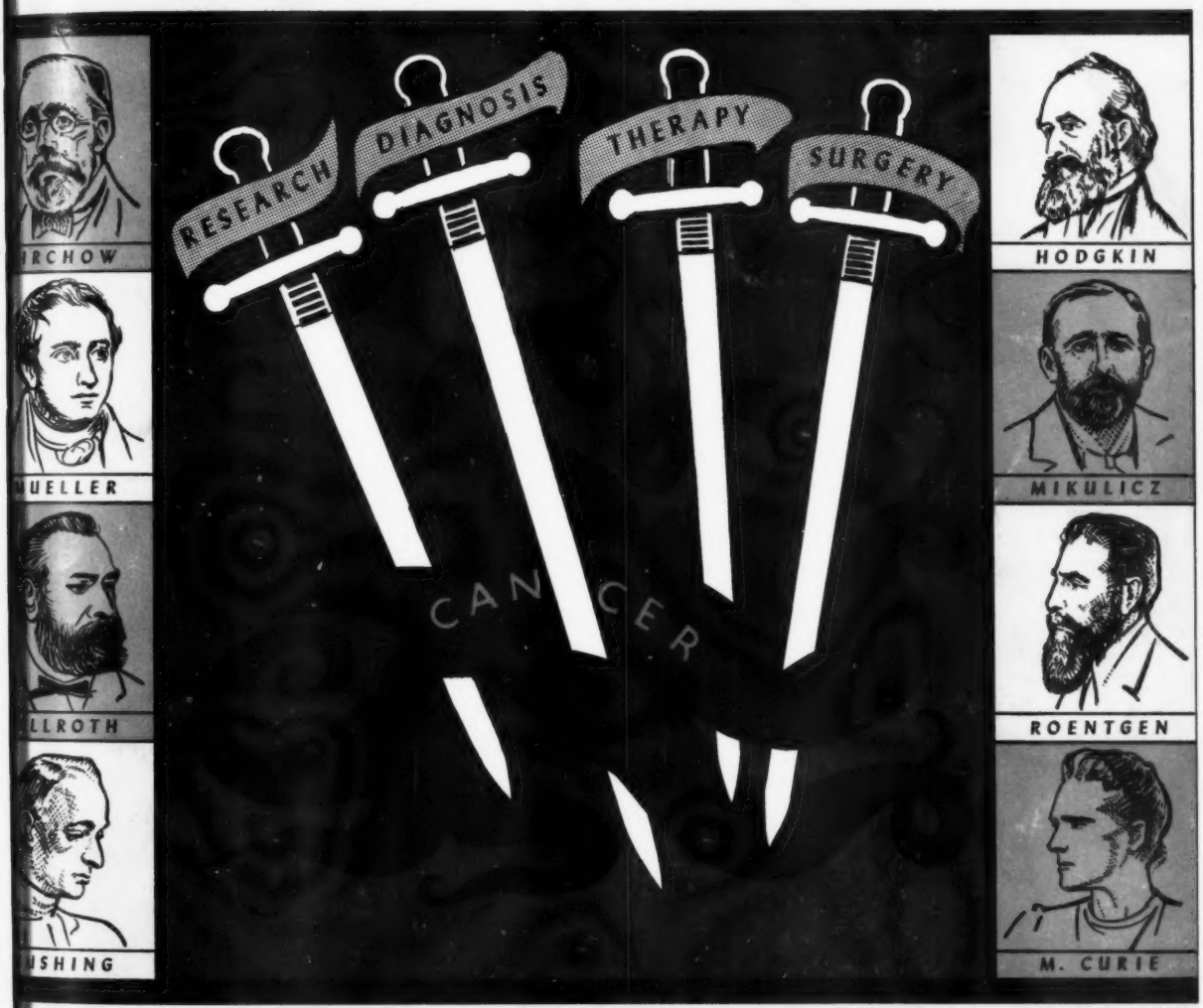

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Disturbances of Gastrointestinal Function Following Partial Gastrectomy

ERIC E. WOLLAEGER*

MAYO CLINIC, ROCHESTER, MINNESOTA

A MAN'S stomach cannot be considered indispensable to him, since he may live for many years after all or most of it has been removed. Indeed, most persons who have undergone extensive resection of the stomach experience surprisingly little, if any, impairment of health as a result of it. The loss of the stomach seems a small price to pay for deliverance from the painful, disabling, and even lethal consequences of neoplasms of the stomach or intractable ulcerating disease of the stomach or duodenum.

A few patients, however, do not fare so well; even though the disease for which they underwent operation has been eradicated, they may suffer from a new set of symptoms attributable to the operation which they have undergone. From a clinical standpoint, it is this small group of patients who do poorly, which stimulates our interest in the disturbances of gastrointestinal function that follow partial gastrectomy.

Some of these patients may complain of loss of weight or inability to gain weight. Others may suffer from the so-called dumping syndrome, characterized by upper abdominal distress immediately after eating, often associated with nausea, vomiting, weakness, palpitation, sweating, flatulence, and diarrhea. Such symptoms usually are transient and mild, but in a few patients they may occur with such frequency and severity as to be almost completely disabling. Some patients may also suffer from abdominal distress and weakness several hours after eating. Although the postgastrectomy symptoms may not be precisely the same in all patients who complain of them, their pattern is sufficiently uniform to suggest that they are caused by or at least related to disturbances of gastrointestinal function brought about by the operation itself.

In considering the various functions of the stomach which might be impaired by partial gastrectomy,[1] only three are pertinent to our present discussion: (1) the reservoir function, (2) trituration of food, and (3) digestion of food. By means of the reservoir function, the stomach retains ingested food during the time that it is being prepared for delivery to the small intestine. This prepared food or gastric chyme enters the intestine intermittently and in small amounts. When the reservoir function is lost, food leaves the stomach rapidly, in large quantities and in an unprepared state.

By means of its triturating function, the stomach breaks morsels of food into fine particles which are easily attacked by the digestive enzymes of the gastrointestinal tract. When this function is impaired, large pieces of food which are not so readily digestible and which may be irritating are passed on to the small intestine. By means of its digestive function, the stomach begins breaking down protein and fat.

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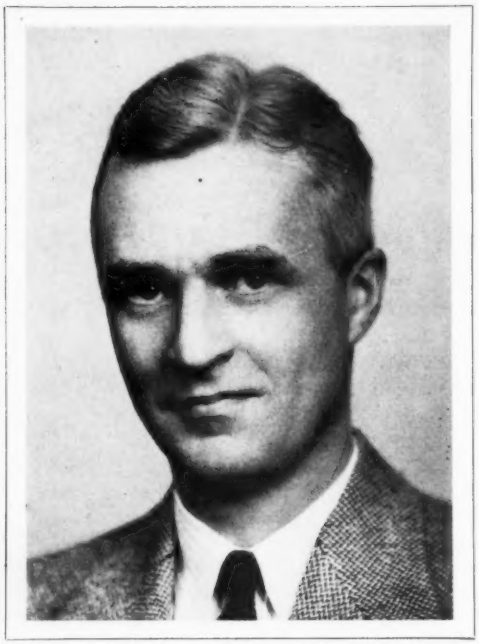

ERIC E. WOLLAEGER

When these three functions are impaired by gastrectomy, an abnormal burden is thrown upon the small intestine, which is forced to deal with large quantities of poorly prepared food materials within short periods of time. In a patient who has undergone partial gastrectomy with a Polya anastomosis (in which the remainder of the stomach [Figure 1] is anastomosed to the jejunum), the burden on the small intestine is further increased by the fact that food leaving the stomach does not pass through the duodenum and is therefore not thoroughly mixed with bile and pancreatic juice high in the intestinal tract. Since the duodenum and upper part of the jejunum have been completely sidetracked by this operation they are not available to help cope with the added burdens imposed by partial or complete loss of gastric function.

Unless the small intestine has the ability to compensate completely for these handicaps, we might expect to find evidence of impaired digestion and absorption among patients who have undergone partial gastrectomy with a Polya anastomosis. In an effort to detect such impairment of gastrointestinal function, my colleagues and I[2] carried out intake-excretion studies of a series of patients who had undergone this operation, measuring the ability to assimilate dietary fat from a standard test diet which had a known composition of fat, protein, and carbohydrate. For comparison, similar studies were made of fat assimilation by healthy subjects who had not undergone operation and who took the same test diet.[3]

The study of each individual extended over a period of several days, and was carried out in a metabolism study unit. The diet was prepared by trained dietitians, and the collection of feces was supervised by nurses familiar with the technics of metabolism studies. The test diet used contained much fat (approximately 200 gm. per day) in order to put to a rigid test the ability of both groups (the group in which operation was performed and the control group) to utilize dietary fat.

Although assimilation of protein was also measured by determining fecal nitrogen, it was found that measurement of fat absorption was a much more sensitive indicator of impaired gastrointestinal function brought about by partial gastrectomy than was that of protein. This might be expected from the fact that there is a special physiologic mechanism which prevents the sudden entrance of large quantities of fat into the small intestine. Of the three major food stuffs, fat is normally retained longest in the stomach. The hormone enterogastrone, one of whose major actions is to inhibit gastric motility, is liberated when fat is placed in the small intestine. The effect of this mechanism is to prevent overburdening of the fat-digesting and fat-absorbing capacities of the small intestine. Its presence suggests that these capacities are more limited in the intact individual than are those for handling protein, for which there is no comparable mechanism.

THE results of our study of fat assimilation are illustrated in Figure 2. Each dot represents the percentage of the fat ingested lost in the feces by one of the controls and each circle represents the percentage of fat ingested lost in the feces by one of the patients who had undergone gastrectomy. They are arranged in order of the degree of fat loss. In every instance except 1, the patients who had undergone gastrectomy lost a greater percentage of ingested fat than did any of the controls. In most cases, the excessive fat excretion was not great, but in 4 cases

the percentage of ingested fat lost was more than twice the maximal loss among any of the controls and in 1 case it was almost seven times this loss. A number of patients who had undergone gastrectomy were studied on diets of moderately low-fat content, and these also were found to lose excessive quantities of fat.

These results indicate the following conclusions:

1. There is impairment of gastrointestinal function following partial gastrectomy with a Polya anastomosis.

2. In most instances the small bowel is able to compensate almost completely for the added burden which the loss of the gastric functions and the sidetracking of the duodenum have thrown upon it. In such cases a rigid test, such as that imposed by the high-fat diet, is necessary to demonstrate the impairment of function.

3. In some instances the small bowel does not compensate so completely, and excessive quantities of fat may be lost in the feces even when a diet only moderately high in fat is ingested. Patients with these greater degrees of steatorrhea are also likely to lose excessive quantities of nitrogen in the feces.

The differences among patients in respect to fecal fat loss following gastrectomy are not readily explainable on the basis of difference in operative technic, since in all cases approximately the same amount of stomach was resected, the same amount of small intestine was sidetracked, and the anastomosis was of the same type and size. Loss of gastric acidity did not alone seem to explain the differences, since some patients with minimal steatorrhea were achlorhydric to the Ewald test while others with relatively great losses of fat secreted some free hydrochloric acid from the remaining portion of the stomach.

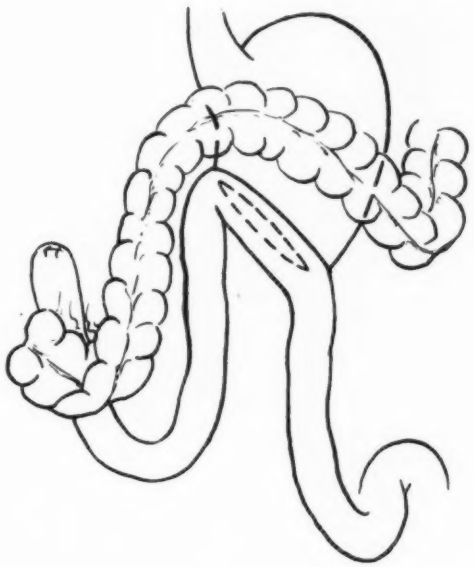

FIGURE 1. Posterior Polya type of anastomosis. (From Wollaeger, E. E., and associates,[2] by permission of Williams & Wilkins Company, publishers.)

It would seem that among various individuals there are rather great differences in ability of the gastrointestinal tract to compensate for the added burden placed upon it by partial gastrectomy with a Polya anastomosis. There are no satisfactory explanations for these differences, unless perhaps they reflect differences in native gastrointestinal endowment. Furthermore, there is no satisfactory way of predicting preoperatively which patients may manifest this lack of compensation.

Evidence concerning the nature of the burden imposed upon the small intestine by partial gastrectomy and the ability of the bowel to compensate for the added load can be obtained from the work of Hertel.[4] This investigator studied digestion and absorption in two series of dogs with fistulas of the small bowel. In one series the fistula was located in the middle portion of the small intestine, and in the other it was located in the terminal segment of the ileum. In both series were included dogs that had not undergone any gastric operation and dogs that had undergone partial gastrectomy.

When the animals with a midintestinal fistula and a partial gastrectomy were given a standard test diet of 100 gm. of meat, the food was soon discharged from the fistula in large amounts and in a very incompletely digested condition. Much of the meat was found to be in relatively large particles which were only partially impregnated with bile and digestive juices. There was also a considerable amount of fluid ejected from the fistula, which often seemed to follow the appearance of meat particles rather than to be mixed with them. Most of the nitrogen-containing material from the fistula was in solid form and little of the total nitrogen ingested as meat protein had been absorbed.

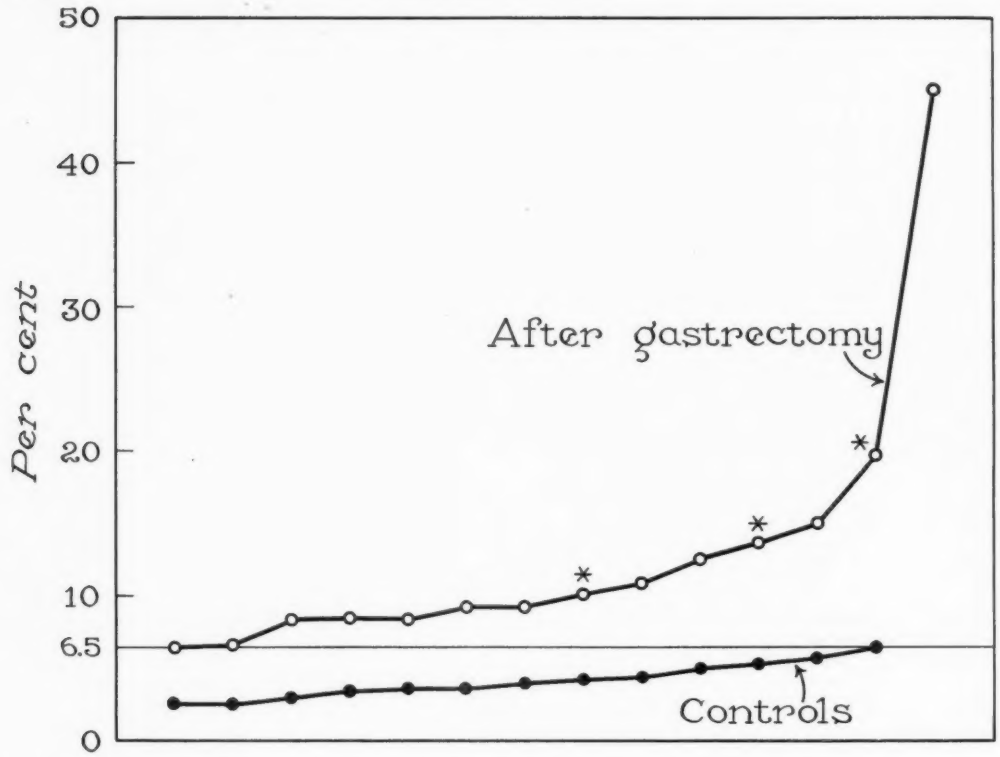

FIGURE 2. Percentage of ingested fat lost in the stools of 27 subjects (arranged in order of degree of loss of fat). The percentages indicated by asterisks represent the highest losses experienced by each of the designated patients in any one period of study. (From Wollaeger, E. E., and associates,[2] by permission of Williams & Wilkins Company, publishers.)

In dogs with intact stomachs, on the other hand, the meat was much more completely digested, and relatively little solid material was discharged from the fistula. The difference between the dogs that had undergone gastrectomy and those with intact stomachs affords clear-cut evidence that partial gastrectomy placed a definite burden upon the digestive capacities of the small intestine.

When gastrectomized dogs with fistulas of the terminal segment of the ileum were fed the same standard meat diet, only a few particles of undigested meat were still recognizable in the discharges from the fistula and they were small. Most of the meat in the test meal had been digested and absorbed. In the dogs with intact stomach, *all* of the meat had been digested and absorbed.

The fact that digestion at the level of the terminal segment of the ileum was almost as complete in the gastrectomized animals as in those with intact stomachs, suggests that considerable compensatory digestive activity had taken place in the lower part of the small intestine of the dogs that had undergone gastrectomy, since these had shown evidence of such poor digestion at the level of the middle portion of the small intestine. The exact nature of this compensatory activity is not known, but part of it at least may concern the motility of the bowel. It seems possible that the rapid passage of the poorly prepared food material through the upper part of the small intestine may be compensated for by a slowing of the rate of passage through the lower part of the small intestine, thus giving an opportunity for more complete digestion and absorption.

The following study indicates that changes in

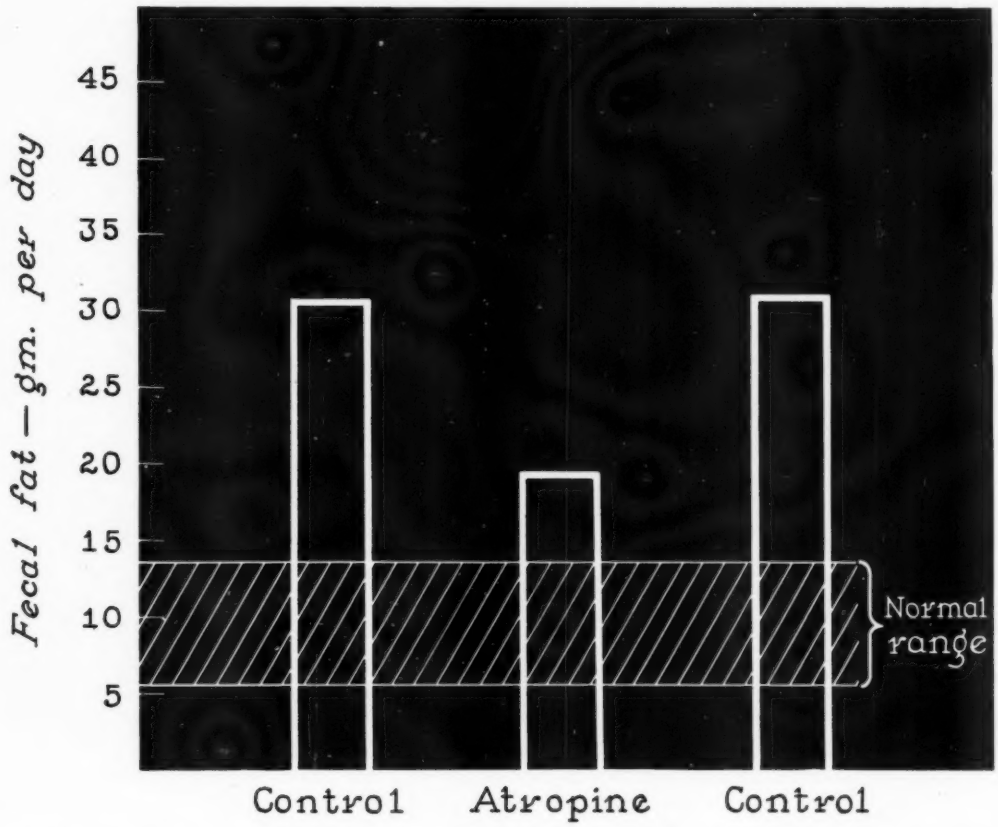

FIGURE 3. The effect of the administration of atropine sulfate upon the fecal fat losses of a patient who had undergone partial gastrectomy with a posterior Polya anastomosis.

intestinal motility may influence the disturbance of digestion and absorption in a patient who has undergone partial gastrectomy. The patient took the standard high-fat test diet during each of three consecutive periods of study (Figure 3). The first and third periods were control periods during which no medication was administered and in each of which he lost approximately 32 gm. of fat in the feces per day. During the second period in which 1/100 gr. (about 0.00065 gm.) of atropine sulfate was administered four times a day by mouth, the fecal fat was reduced to 19 gm. per day. Although a single study of this sort does not constitute proof, it strongly suggests that abnormal motility of the bowel (which was presumably reduced by the atropine) played a role in bringing about the steatorrhea in this case.

Further support for the idea that abnormal gastrointestinal motility plays a role in the pathogenesis of steatorrhea is obtained from the following study of a patient with insufficiency of external pancreatic secretion due to chronic pancreatitis associated with diabetes and diffuse calcification of the pancreas.

The patient took a standard diet of moderate fat content (approximately 100 gm. per day) throughout the study (Figure 4). During the first control period his fecal fat losses were about 39 gm. per day. When he was given 1/150 gr. (about 0.00043 gm.) of atropine sulfate subcutaneously before meals, the fat losses dropped to 19 gm. per day. In the third period, in which he was given 5 gm. of pancreatin with each meal, the fecal fat was 12 gm. per day. In the fourth period, in which no medication was

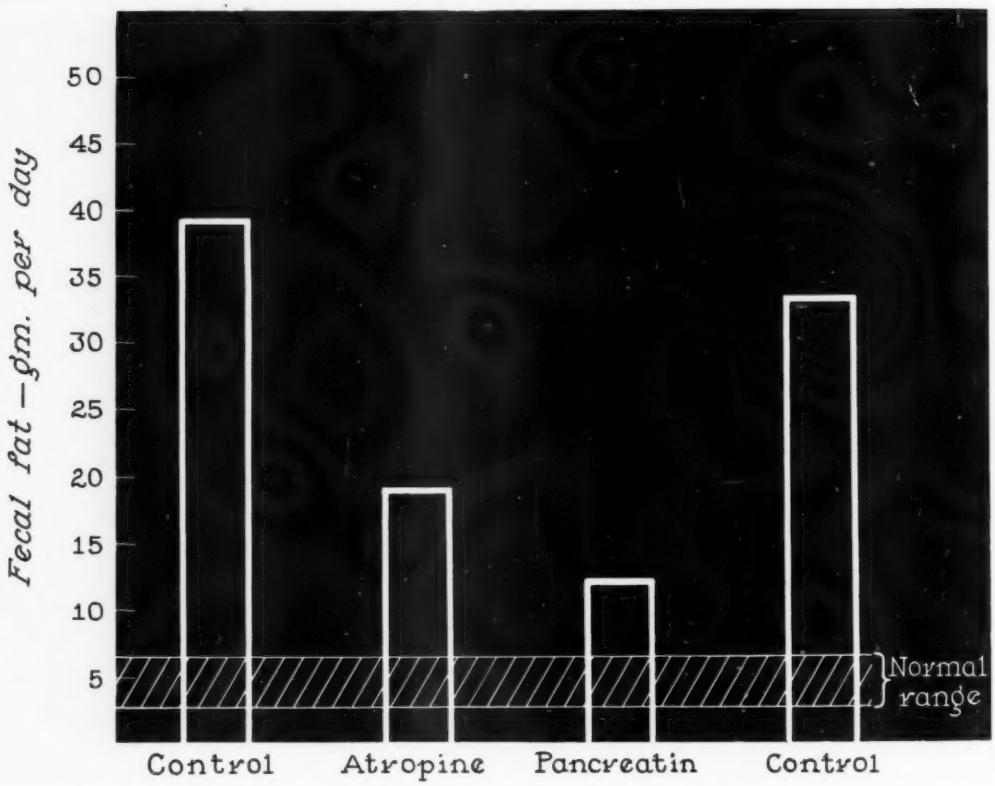

FIGURE 4. The effect of the administration of atropine sulfate and of pancreatin upon the fecal fat losses of a patient with insufficiency of external pancreatic secretion due to chronic pancreatitis.

given, the fecal fat increased to 33 gm. per day.

In this case, even though the primary defect was a lack of the digestive juice of the pancreas, the change in gastrointestinal motility which the administration of atropine presumably brought about resulted in a substantial reduction of the degree of steatorrhea. The abnormal motility in this case may well have been caused by the presence of large amounts of poorly digested food material which the small bowel was forced to handle. As pointed out previously, large amounts of poorly digested food are also found in the small bowel after partial gastrectomy. Whether or not the flow of digestive juices from the pancreas and liver is normal in amount and quality after partial gastrectomy is not definitely known. However, there is good reason to believe that in such cases admixture of these juices with ingested food is not thorough and does not take place as high in the intestinal tract as it does in the intact animal.

In an attempt to elucidate the cause of the steatorrhea following partial gastrectomy, my colleagues Drs. Comfort, Waugh, and Power collaborated with me[5] in studying a series of patients who had undergone partial gastrectomy with a Billroth I type of anastomosis, in which the remainder of the stomach is joined to the duodenum rather than to the jejunum (Figure 5). In this group of patients the resection of stomach had been equally extensive as in the group with Polya anastomosis—that is, from one-half to two-thirds of the stomach had been removed in each case. The same high-fat test diet was administered which had previously

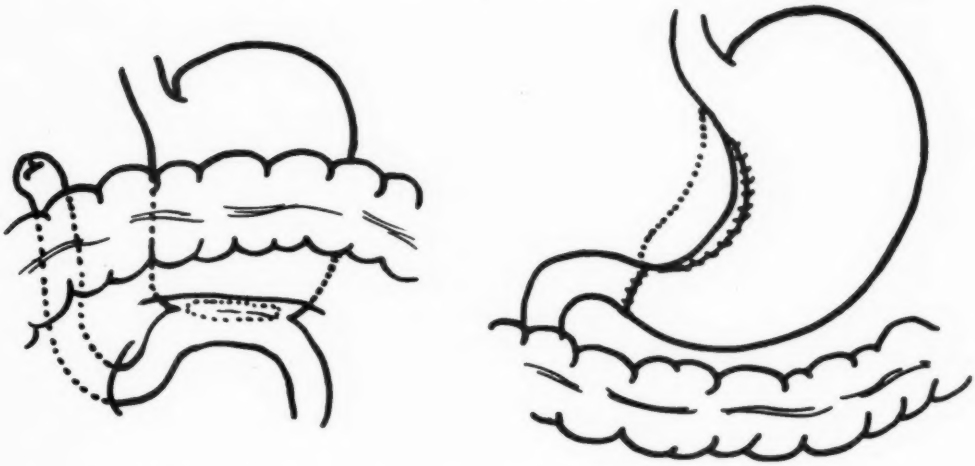

FIGURE 5. Posterior Polya type of anastomosis (left side); Billroth I type of anastomosis (Schoemaker modification) (right side).

been employed in the study of the Polya group and the controls.

The mean fecal fat among the 13 controls was 8.7 gm. per day. The mean among the 8 patients with a Billroth I anastomosis was 12.3 gm. and among the 10 patients with a Polya anastomosis it was 19.9 gm. per day. The difference between these means was found to be statistically significant. This evidence leads to the conclusion that partial gastrectomy with anastomosis of the remaining portion of the stomach to the duodenum is followed by less disturbance of gastrointestinal function than is partial gastrectomy with anastomosis to the jejunum, even though the same amount of stomach has been resected.

BOHMANSSON'S[6] studies brought him to a similar conclusion. He attributed the advantage of the Billroth I operation to two factors: First, the stomach empties into the duodenum, thus allowing food material to be mixed with bile and pancreatic juice high in the intestinal tract and taking maximal advantage of all the digestive and absorbing capacities of the small intestine. Second, after a Billroth I operation the stomach tends to empty in a more normal manner (that is, intermittently and at a slower rate) than it does after a Polya operation. He cited roentgenoscopic evidence to support the presence of this second factor. The significant difference in degree of steatorrhea between the patients with a Billroth I anastomosis and those with a Polya anastomosis seems to minimize the importance of the amount of stomach removed (which was the same in both groups) and emphasizes the importance of the site of anastomosis and manner of gastric emptying.

From these studies concerning the disturbances of gastrointestinal function following partial gastrectomy, can we derive any worthwhile information about the genesis of the postgastrectomy symptom? We can at least make a few conjectures. It seems likely that the sudden entrance of relatively large amounts of poorly prepared food material into the bowel would stimulate intestinal motor activity to an abnormal degree and that this might be sufficient to cause abdominal distress in some patients.

That stimulation of excessive peristalsis occurs is suggested by the crampy abdominal pain, the borborygmus, and the evidence on roentgenoscopic examination of a rapid transit of intestinal contents into the lower reaches of the small intestine. The nausea of which many patients complain suggests reverse peristalsis and might be an evidence of compensatory intestinal activity, the effect of which would be to slow the passage of food material. Certainly there is much to suggest that the stimulus for the dumping symptoms may be increased motor activity of the intestine, perhaps disordered and perhaps

TABLE 1

RELATIONSHIP OF DIGESTIVE SYMPTOMS TO DEGREE OF FAT LOST IN THE FECES AMONG PATIENTS WHO HAD UNDERGONE PARTIAL GASTRECTOMY WITH A POSTERIOR POLYA ANASTOMOSIS*

PATIENTS WITH MILD OR NO DIGESTIVE SYMPTOMS			PATIENTS WITH SEVERE DIGESTIVE SYMPTOMS†		
PATIENT	GROUP	PER CENT INGESTED FAT LOST IN FECES	PATIENT	GROUP	PER CENT INGESTED FAT LOST IN FECES
1	1	9.5	4	1	11.0
2	1	8.3	5	1	15.1
3	1	6.6	6	1	9.4
7	1	8.3	10	1	12.5
8	1	6.5	11	2‡	12.7§
9	1	8.2	12	2	15.0§
			13	2	9.2§
			14	2	45.2
Range		6.5-9.5	Range		9.1-45.2

*From Wollaeger, E. E., and associates,[2] by permission of Williams & Wilkins Company, publishers.
†Only one patient (patient 5, group 1) gave clinical evidence of recurring peptic ulceration.
‡The patients of group 2 were given diets of which the fat content was less than that in the diet given to group 1.
§Average of loss in multiple periods of study.

compensatory in nature, resulting from the added burden thrown upon the bowel by the loss of normal gastric function.

Secretory activity may also be stimulated to an abnormal degree by the sudden entrance of relatively large amounts of poorly prepared food material into the upper part of the intestine. The increased volume of the intestinal contents due to secreted fluid would in itself act as a stimulus to intestinal motor activity. Machella[7] has recently emphasized the role of hypertonic foods in producing the dumping symptoms by causing increased secretion of fluid into the intestinal lumen.

There is some relationship between the degree of impairment of gastrointestinal function and the severity of postgastrectomy dumping symptoms. This is indicated by the data of Table 1 from patients who had undergone partial gastrectomy and a posterior Polya anastomosis. The 6 patients listed on the left half of the table complained of very mild symptoms or none at all. They lost in the feces between 7 and 10 per cent of the fat ingested. The 8 patients listed on the right half of the table complained of more severe postgastrectomy symptoms. The fecal fat losses in this group ranged between 9 and 45 per cent of the fat ingested and in all but 2 instances the losses were well over 10 per cent.

This evidence fits in with the clinical impression of my colleagues and me that the incidence of severe dumping symptoms among patients who have undergone a Billroth I anastomosis is considerably less than it is among those who have undergone a Polya anastomosis. As pointed out previously, the former operation is also followed by a lesser degree of steatorrhea.

So far as loss of weight is concerned, it seems clear that the excretion of abnormal amounts of fat and nitrogen in the feces might contribute to this symptom. However, in most instances the degree of steatorrhea is small and in only a few individuals does it seem enough to be of major importance from the standpoint of loss of calories. More often loss of weight is due to a reduction of food intake in an effort on the part of the patient to avoid postprandial distress.

THERE are unquestionably other factors involved in the production of postgastrectomy symptoms than the degree of impairment of gastrointestinal function, as demonstrated by intake-excretion studies of fat. The severity of the dumping symptoms may vary in the same patient from one day to the next, even when

exactly the same food is ingested. These variations may be due to differences in fatigue, nervous tension, or other unknown factors.

In collaboration with Dr. Grace Roth, I once attempted to study the pulse rate, blood pressure, and skin temperatures of a series of patients with the dumping syndrome, thinking that a vascular reflex might be responsible for the symptoms. All of the 6 patients studied insisted that they habitually experienced severe symptoms every time food was eaten. Each patient was given in a test meal a liberal quantity of the type of food he had previously found to be most upsetting to him. The studies were carried out early in the day under fasting conditions with the patients in the sitting position. After suitable baselines had been established, the test meal was eaten, after which not one of the patients experienced any symptoms whatsoever. This is a strong indication, it seems to me, of the importance of a nervous factor in the production of the dumping symptoms. The fact that the patient has undergone partial gastrectomy may set the pattern for his symptoms, but other factors may influence the incidence, frequency, and severity of them.

SUMMARY

Partial gastrectomy usually brings about some impairment of gastrointestinal function as measured by intake-excretion studies of fat. This impairment is probably due to reduced gastric function and to the inability of the small intestine to compensate completely for the added burden thrown upon it. The impairment of gastrointestinal function is usually not great, but in a few instances it may be of considerable magnitude. It tends to be greater among patients who complain of postgastrectomy symptoms than in those who have no such symptoms. Evidence has been presented which suggests that abnormal motility of the gastrointestinal tract plays a role in the pathogenesis of the steatorrhea that follows partial gastrectomy.

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Diagnostic Clinic

Carcinoma of the Large Bowel

W. WAYNE BABCOCK*

TEMPLE UNIVERSITY SCHOOL OF MEDICINE, PHILADELPHIA

INTESTINAL cancer is the second most common and the most curable internal cancer. It has a much more favorable operative prognosis than cancer of the stomach, pancreas, gallbladder, lung, uterus, prostate, bladder, or kidney. But a most distressing feature is the delay in diagnosing the disease, a delay which now averages seven months or more. During this delay about 20 per cent of the patients develop a hopeless extension of the disease to the liver or other ineradicable parts of the body, and statistics show that 25,000 persons in the United States are now dying yearly from this disease. It seems probable that an earlier diagnosis, of say three or four, instead of seven months after the first symptoms, could enable several thousand of the 25,000 now dying to be saved yearly. Many persons are now living in good health ten to twenty years after radical operations for cancer of the bowel, but the number is not nearly as large as it should be. Who is to blame for this delay?

Possibly the development of watertight specialties may favor oversight as to the presence of intestinal carcinoma. I recently asked a specialist if he ever made a rectal examination. "No," he replied, "I am a gynecologist, and gynecologists do not examine the rectum." But we are largely blamable for not educating the practitioner as to the characteristics of and proper methods for diagnosing carcinoma of the intestine. Many graduates have never palpated a rectal carcinoma and there is a general impression that tumors of the bowel always require a roentgenologic examination, and that a biopsy is essential to establish the diagnosis. What are the facts?

Ninety-seven per cent of all intestinal cancers occur in the large bowel and about 70 per cent are located in the rectum and lower sigmoid where they may be reached and diagnosed by the finger or proctoscope.

Cancers of the cecum and ascending colon usually are bulky, but not obstructive and they tend to bleed and necrose with resulting anemia and cachexia. A large proportion are palpable through the anterior abdominal wall. Cancers of the left half of the colon usually form a rather narrow ulcer which tends to encircle the bowel. The ulcer has raised, everted, indurated borders. The diameter of the bowel may not be increased and the outside of the bowel shows an annular groove as if a string had been tied tightly around the gut. From their small bulk and deep location in the abdomen these leftsided growths as a rule are not palpable through the anterior abdominal wall. They cause obstructive symptoms, and the painful, colicky contractions of the proximal section of colon have led to the removal of the gallbladder or appendix.

In the lower sigmoid and in the rectum larger lateral growths predominate. Beginning usually as a papilloma with a broad base, the center of the growth undergoes necrosis and ulcerates forming a depression or crater with surrounding raised, everted, scalloped borders that have an induration extending into the underlying

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Presented November 1, 1949, before the meeting of the Interstate Postgraduate Medical Association of North America, Philadelphia, Pennsylvania.

intestinal wall. I know of no other ulcer that has these physical characteristics and when present they enable the diagnosis of carcinoma to be made by the examining finger with an accuracy equal to that of a biopsy. This common type is symptomless until necrosis and ulceration lead to the presence of blood and abnormal amounts of mucus in the stools, when the patient often is treated for bleeding internal piles. The general health of the patient is usually not affected until complications develop. The rarer villous form of carcinoma causes a profuse watery and mucous diarrhea. Carcinoma so frequently develops from a papillary or polypoid colitis that early excision and biopsy of these growths, as well as of benign appearing villous growths, should be practiced.

In about 16 per cent of the patients with intestinal cancer multiple lesions are present. These may be primary or in part seedlings from a primary growth. Only about 2 per cent of intestinal tumors involve the anus, usually as an epithelioma characterized by much pain and tenesmus and often mistaken for a benign fissure or ulcer. Otherwise intestinal carcinomas are essentially painless except as they develop complications such as obstruction or perforation.

With a knowledge of the manifestations of intestinal malignancies the physician can intelligently develop the patient's history and, after a general, an abdominal and a rectal examination, in most cases make an accurate diagnosis as to the situation, and malignancy of the common carcinomatous tumors lying below the midsigmoid. Apparently many practitioners believe that the diagnosis can be made only by x-ray examination, and I have seen nearly 70 patients whose operation was delayed for months because they were first referred to radiologists. The common rectal cancer lying within the pelvis rarely shows on the x-ray film, the soft tissue lesion being obscured by the surrounding bony pelvis, so that for these patients the report had been "no evidence of carcinoma."

For the 30 per cent of colonic cancers lying above the pelvis, the x-ray is the most valuable method of diagnosis. For cancer involving the rectum and lower sigmoid the diagnosis is best made by the finger or proctoscope. After a digital examination an x-ray study may be found desirable to develop details as to an abdominal mass or to locate metastatic lesions in bones or other parts. The mistake has occasionally been made of giving barium by mouth when an intestinal cancer is present. Obviously this will obscure the tumor and may precipitate an intestinal obstruction.

W. WAYNE BABCOCK

Clinical features of these tumors are illustrated in the figures accompanying this paper.

CASE REPORTS

In a 50-year-old man, a firm, somewhat movable mass the size of a baseball was outlined in the lower right quadrant. He had been losing weight and becoming pale for six months, but had noticed no other symptom. The removed right half of the colon was opened revealing a rather soft necrotic and hemorrhagic mass in the cecum, characteristic of cancer of the right half of the colon.

By opening the abdomen of a man of 38 years we exposed a narrow groove encircling the upper sigmoid. The bowel was not enlarged and the mass was too small to be felt through the overlying abdominal wall. When we split the bowel open, the groove was seen to lie over an annular ulcer with upper and lower narrow, raised, and everted borders. This is the typical

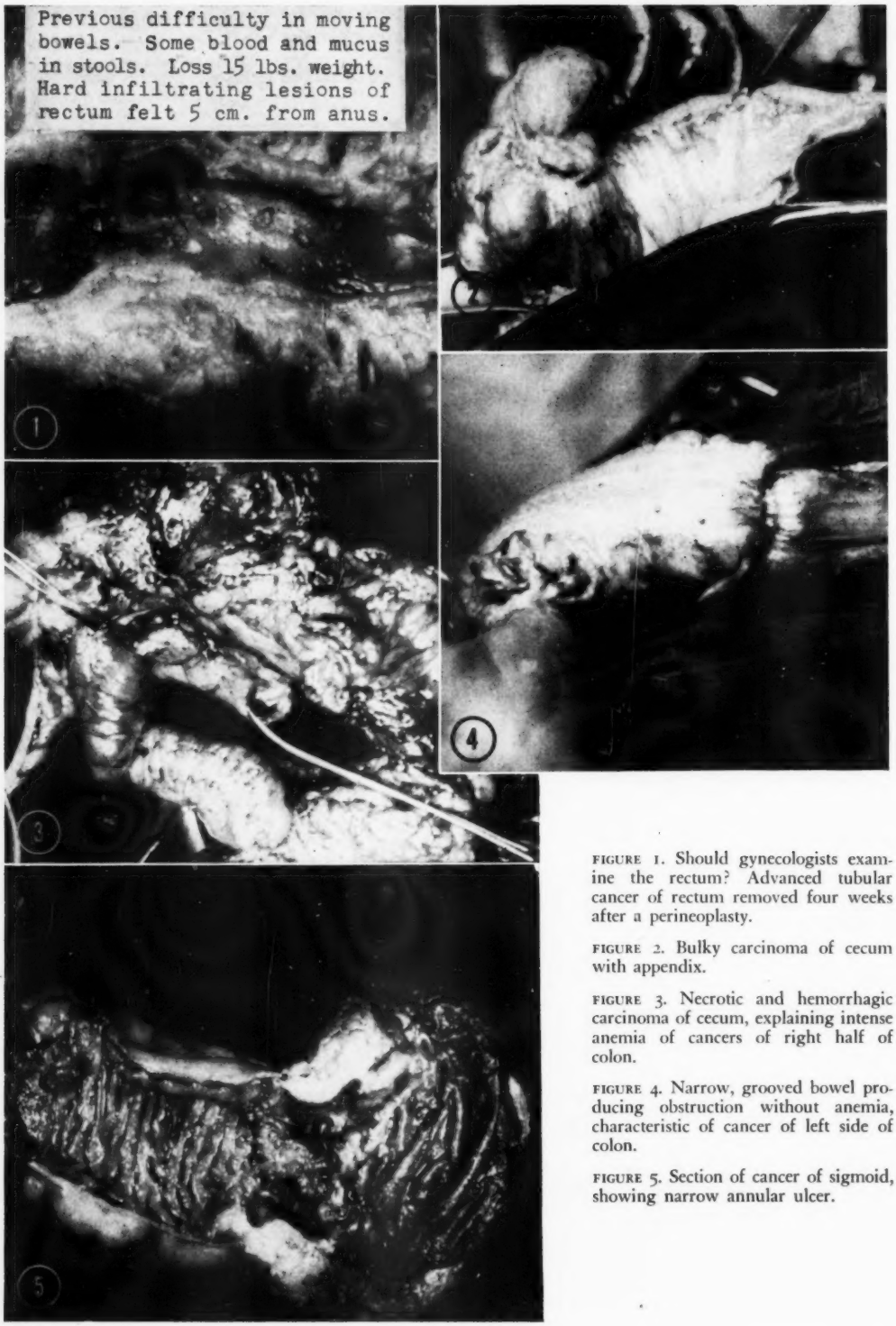
Previous difficulty in moving bowels. Some blood and mucus in stools. Loss 15 lbs. weight. Hard infiltrating lesions of rectum felt 5 cm. from anus.
1
2
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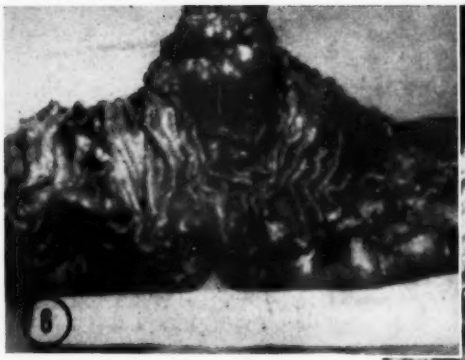
FIGURE 1. Should gynecologists examine the rectum? Advanced tubular cancer of rectum removed four weeks after a perineoplasty.

FIGURE 2. Bulky carcinoma of cecum with appendix.

FIGURE 3. Necrotic and hemorrhagic carcinoma of cecum, explaining intense anemia of cancers of right half of colon.

FIGURE 4. Narrow, grooved bowel producing obstruction without anemia, characteristic of cancer of left side of colon.

FIGURE 5. Section of cancer of sigmoid, showing narrow annular ulcer.



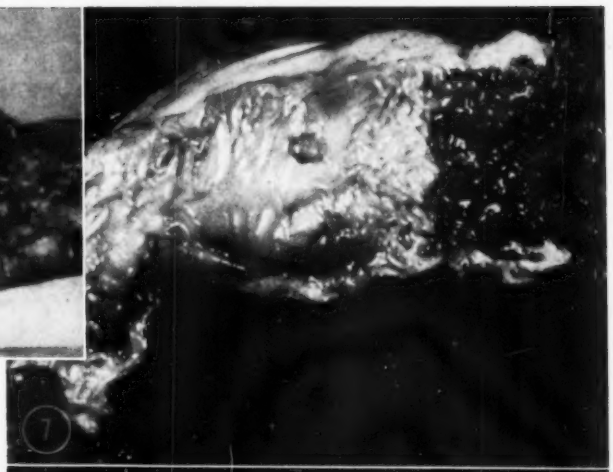


FIGURE 6. Papillary cancer of sigmoid.

FIGURE 7. Extensive ulcerating rectal carcinoma *(right)*; small papillary cancer *(center)*; two large papillary cancers with beginning umbilication *(left)* to rectum and sigmoid.

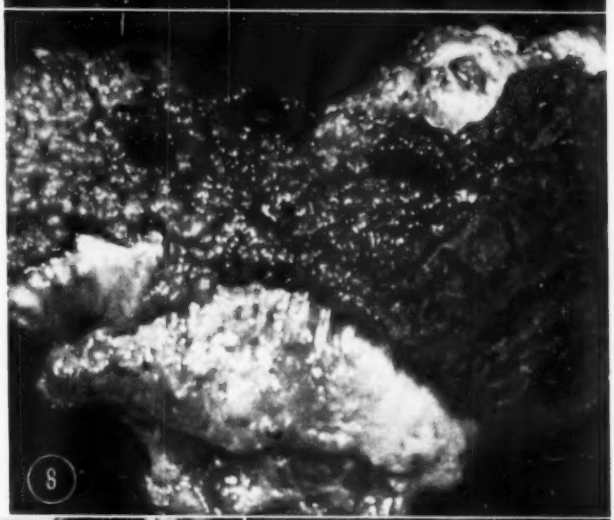


FIGURE 8. Diffuse papillary colitis with cancers and hepatic metastasis in a man of 28 years.

FIGURE 9. Cancer of cecum invading loop of ileum. Combined single stage resection. No evidence of recurrence after three years.

FIGURE 10. The highly malignant epithelioma of anus often mistaken for simple fissure or ulcer.

appearance of the usual cancer of the left half of the colon above the midsigmoid, and the patient had complained of rightsided abdominal colic with constipation.

In another instance, a section of the rectum showed multiple cancers in various stages; several were minute and nodular; there was a small firm rounded papilloma with smooth surface and broad base; a more advanced papilloma with top evacuated by ulceration, and the usual well-developed stage with a rather large, smooth excavated crater, extending through the muscular layers and surrounded by a raised, scalloped everted border of hard malignant tissue. Such an ulcer can easily be recognized as malignant by the examining finger. Apparently this was the primary cancer with satellite implants in the adjoining mucosa. As the large ulcer had invaded vascular layers the liver should be examined for metastatic growths. The patient had had bloody and mucous stools for eight months, but x-ray examinations had been negative.

In still another case, the patient had three annular carcinomas of the transverse colon, all with about the same degree of development. There were characteristic secondary growths in the liver. On the surface they projected slightly, had a yellowish or grayish color and a rounded or slightly umbilicated surface. As one grasps such a liver between the thumb and fingers, rounded firm malignant masses may often be detected deep beneath the surface. In 676 radical colonic resections for cancer I found metastatic growths in the livers of 97 patients. Twenty-one of these 97 patients have lived three years; 8, five years; 3, ten years, and 1, twelve years after the operation. In contrast, only 4 patients with marked gross involvement of the lymphatics tributary to the growth have lived over five years. Obviously hepatic metastasis should rarely contraindicate the removal of the primary tumor.

Diverticulitis and other inflammatory or benign masses may be mistaken for an ineradicable malignancy. It is important therefore that a diagnosis of a hopeless malignancy not be accepted without dependable laboratory proof.

For example, a patient had had five operations in the belief that there was malignancy present, and finally it was considered to be incurable. She had fistulas of the large and small bowel through a wide scar, and although an "appendectomy" had been reported years before there was a chronic perforated leaking appendix high up under the right kidney. This had caused the marked thickening of the bowel, fistulas and cachexia, which led to the belief that cancer was present. In 2 other patients with diverticular masses diagnosed as carcinoma a palliative colostomy had been used for a supposed hopeless condition.

When an intestinal cancer has perforated with the formation of a localized abscess, should we delay the removal of the malignant tissue while an attempt is made to eliminate the abscess? Surely there should be no long delay, and it is obvious that the infection cannot be eliminated without removal of the malignant growth.

In one very obese patient a large abscess had developed in the thick abdominal wall from a colonic cancer, and this had been drained for four months, had then closed to return two or three months later. By a very wide excision it was possible to remove a large section of the abdominal wall and attached colon with the abscess intact, and perform an aseptic end-to-end anastomosis of the colon, without wound infection.

Frequently the colonic cancer has invaded other intestinal segments which should be removed with the primary growth. A patient had a carcinoma of the cecum that had involved a large loop of ileum, so that the right colon, together with the lower two meters of ileum were removed en masse with an end-to-end aseptic anastomosis and the patient has remained in good condition for three years postoperatively.

OPERATIVE PROCEDURE

The operation we have used depends on one's ability to pull a section of normal sigmoid with its mesentery through the pelvic floor. To do this we must straighten the sigmoid loop by dividing the superior hemorrhoidal vessels, which act like the string of a bow. These vessels are divided usually just below the first sigmoid loop. Then, as the loop opens up, there is in most cases a sufficient length of bowel to reach through the pelvic floor. In the average adult it requires about 12 cm., or 5 inches, of colon to run from the promontory of the sacrum through the anus.

In doing this operation the abdomen is opened and explored for any secondary growth; then the sigmoid is turned to the right and any attachments of the sigmoid on the left side are divided, as well as the left lateral leaflet of the

sigmoid. This exposes the left ovarian or spermatic veins, which are freed from the peritoneum. Medial to the veins lies the left ureter, which likewise is liberated well into the pelvis.

A hand is then introduced back of the rectum and sigmoid and the entire mass separated from the underlying vessels and vertebrae, and then the hand is carried over the brim of the pelvis and the rectum separated from the sacrum. The peritoneum on the right side is divided just medial to the right ureter and the upper superior hemorrhoidal vessels caught up on the finger, doubly ligated and divided. Peritoneal and fascial incisions are made wide of the growth and around the pelvic brim, and the growth liberated with division of the lateral pedicles of the rectum, containing the lower hemorrhoidal vessels at the sides of the pelvis.

A folded gauze tape is then tied around the liberated bowel at its lowest level of vascularity, and the upper sigmoid and lower descending colon sufficiently liberated for normal colon to reach through the pelvic floor. The folded gauze tape is packed against the floor of the pelvis to stop oozing and to be a guide in the later stage of the operation. For radicability so much peritoneum and fascia propria have been removed that one cannot form a pelvic diaphragm or cover the vertebrae, nor is this necessary.

We have now liberated the bowel to the floor of the pelvis and have an attached pack of gauze tape underneath. The next step is to close the abdominal wound, for which I use interrupted or continuous layer sutures of stainless steel wire. This suture material provides security against disruption with minimal reaction in the wound.

At the completion of the abdominal stage we put in a suction or sump drain to the bottom of the pelvis. This gives us a guide, first, as to secondary bleeding; second, by a sudden flow of serum to a secondary ileus and obstruction. This serum appears twenty-four or forty-eight hours before vomiting or abdominal distention develops; third, to any septic condition developing in the abdomen shown by the character of the material that is aspirated through the stainless steel tube.

The final step of the operation is to remove the diseased bowel through the split anus. With the patient in the lithotomy position and the rectum packed with gauze wet with tincture of iodine, a midline incision is made through the posterior border of the anus to the base of the coccyx. With retraction, the ligaments attaching the coccyx anteriorly and on the right side are divided, and the levator muscles elevated on each side on the finger and divided wide of malignant infiltration. The bowel is then divided at the junction between the rectum and the anal canal. As it is cut the rectum is grasped successively by forceps, and withdrawn. Iodine has the advantage over mucous surface antiseptics in that it stops the flow of mucus from the glands and leaves a dry mucosa.

The withdrawn 25 to 50 cm. of colon are wrapped in a towel and laid over the pubis. With the aid of a gynecologic trowel the cavity of the pelvis is studied, bleeding controlled, and the perineal wound lightly closed in layers with all-steel wire. Layer 32 and 35 gauge interrupted sutures are introduced and tied.

Having closed the wound with care not to constrict the bowel, dressings are applied, a rectal tube tied in the bowel, and redundant bowel cut away.

At the end of a week, the perineum is usually healed; the rectal tube has loosened and slipped out, but 7 to 10 cm. of living bowel protrude. No sutures have been used to sew the bowel to the skin or other tissue because the longitudinal peristaltic waves would then tend to tear holes in the bowel. In the operation the bowel is never sewed to any surrounding structure; it lies free until it attaches itself.

At this time, or a little later, a rectal tube is again introduced and an ordinary tonsil snare applied about 1 or 2 cm. beyond the skin margin. My associate, Doctor Jonas, has found that if the bowel is constricted for five minutes it may then be cut away without any bleeding. After twenty or thirty minutes the stump then retracts into the anus spontaneously and heals without suture.

The scar in the raphe is almost invisible after some months and patients are able to control the sphincters. Control is adequate for solid movements but rarely for liquids without a secondary plastic. However, of 127 patients questioned, only 3 were dissatisfied with their results.

For cancer of the abdominal colon wide resection and end-to-end anastomosis with or without a temporary colostomy or appendicostomy has supplanted other operations. We now recognize that rectal cancer spreads upward and laterally. Observations, as you know, made by many persons during recent years have shown

TABLE 1
PERCENTAGE OF PATIENTS SURVIVING FIVE AND TEN YEARS AFTER 676 RADICAL OPERATIONS

TYPE OF OPERATION	NUMBER OF PATIENTS	SURVIVED FIVE YEARS, PER CENT	SURVIVED TEN YEARS, PER CENT
A.P.P.S.[1]	302	77·3	47
P.P.S.[2]	101	20	10
End-to-end	191	59	41
Mikulicz-Rankin	82	40	21

[1]A.P.P.S.: Abdomino-perineal proctosigmoidectomy.
[2]P.P.S.: Perineal proctosigmoidectomy.

that the downward spread is very slight, and for twenty years we have been re-examining patients who had had the bowel pulled through the perineum, to see if in any of them any residual cancer tended to grow toward the anus. I have not seen a single case in which residual cancer of the pelvis has shown such a tendency.

The relation of longevity to the type of operation used is important. That it has been better from the pull-through operation than that reported by various operators for the Miles operation, I attribute to the free removal of peritoneum and fascia propria which in the Miles operation is retained to peritonealize the posterior abdominal wall and to form a pelvic diaphragm.

The relation of postoperative longevity to the type of operation used is important (Table 1). The shortest longevity followed perineal or perineo-abdominal resections for cancer of the anus and adjacent rectum. In this region the tumors are not only highly malignant but have lymphatic extensions, especially about the thighs, to the medial inguinal lymphatics which are difficult to eradicate.

The second shortest survivals have followed the Mikulicz-Paul exteriorization operation, which, especially for the sigmoid and rectum, lacks radicability.

Recurrences of the cancer in the abdominal scar led Rankin to adopt an obstructive resection in which the malignant loop of bowel was immediately removed. However, cancer may also be implanted in the abdominal wall because of the difficulty, in this type of operation, of exteriorizing and removing all of the malignant bowel and mesentery.

By the time the recurrence in the abdominal scar is evident, the cancer has in our experience always become ineradicable. A one-stage resection with immediate end-to-end anastomosis of the bowel enables a much more radical excision, a short period of hospitalization, and relative freedom from cancer implantation in the wound; therefore we believe that the Mikulicz operation should never be used except to bridge an emergency.

That the five-year survival rate (59 per cent) after end-to-end resection and anastomosis has not been as good as that following the abdomino-perineal resection, may be attributed to the possible wider lines for malignant diffusion from abdominal as compared with pelvic cancer.

COMING POSTGRADUATE COURSES

American College of Physicians

Recent developments in medicine, November 6-11, at University of Utah College of Medicine, Salt Lake City, M. M. Wintrobe, M.D., Director

Peripheral vascular diseases including hypertension, November 27-December 2, at Mayo Clinic and Mayo Foundation, Rochester, Minn., Walter F. Kvale, M.D., Director

Gastroenterology, December 4-9, at University of Pennsylvania Graduate School of Medicine, Philadelphia, Henry L. Bockus, M.D., Director

Selected aspects of clinical hematology, December 11-16, at New England Center Hospital and Tufts College Medical School, Boston, William Dameshek, M.D., Director

Modern trends in diagnosis and treatment of heart disease, January 22-27, 1951, at Woman's Medical College of Pennsylvania and other Philadelphia institutions, William G. Leaman, Jr., M.D., Director

University of Kansas School of Medicine, Kansas City

Psychosomatic medicine, October 30-November 1, at Winter V. A. Hospital, Topeka

Obstetrics, gynecology and pediatrics, November 6-10

Therapeutics, December 11-13

Radiology, January 8-10, 1951

Surgery, including urology, orthopedics and industrial surgery, January 29-February 2, 1951

Continuation type course in general practice, October 19-April 19, afternoon and evening sessions, third Thursday of each month

Electrocardiography, January 18-March 1, continuation type course, all-day program on Thursday—6 weeks

Diagnostic Clinic

The Prognosis in Coronary Heart Disease

WILLIAM G. LEAMAN, JR.*

WOMAN'S MEDICAL COLLEGE OF PENNSYLVANIA, PHILADELPHIA

I WOULD like to discuss some impressions regarding the prognosis in coronary heart disease which I have gleaned from a recent review of office records covering a period of about 17 years as a consultant in this so-called specialty of cardiology. I propose to omit slides showing the charts and percentage tables and sequence of electrocardiograms. I do this in order to cover fundamental points and particularly to show 2 patients who illustrate these points.

First, a few remarks regarding our topic as a whole. Obviously, statistics on prognosis will vary according to the type of cases studied. Should we analyze a series of cases from a large hospital, we would obtain a much darker view than we would if we studied a similar number of ambulatory patients, the patients who come into the consulting room of the internist.

While this presentation attempts to strike an optimistic note, I realize at the start that I would be rather foolish to overlook the fact that some patients die suddenly in their first attack. Others (about 10 per cent in our series) may never have chest pain and if the pain equivalent is missed, this group may not be diagnosed. Finally, others who have coronary disease may only be diagnosed at necropsy at a ripe old age and may die noncardiac deaths. Consequently, tables of percentages are apt to be inaccurate for these reasons. Statistics don't lie, but I think there is an old adage to the effect that liars can use statistics.

The prognosis in coronary disease must be assessed on the basis of all the facts obtainable from each patient. That is the reason we are in the practice of medicine. Every patient is different, as you will see in a few moments.

We will first of all direct our attention to the prognosis of the attack of acute myocardial infarction. The immediate mortality averages 30 per cent. It is higher in the second and third attacks (about 50 per cent). In persons 50 years of age or older, the immediate prognosis is poorer than in those under 50. That much I know from my acquaintance with the coroner's physician. In the colder months in Philadelphia he tells me that the incidence is high. However, considering the group as a whole, we find that 75 per cent of the attacks occur during complete inactivity.

There are certain symptoms that one can recognize at the bedside. There is often dyspnea which is associated with a cold, clammy appearance. If the pain is in the upper substernal area, or anywhere, as the late Richard Cabot said, "within a foot of the heart," associated with effort, and if this pain recurs after the initial attack with more severity, the prognosis is influenced adversely. Older patients who have a clouded sensorium (disoriented patients) do poorly.

The presence of congestive failure lessens the chance of survival. Of course, one swallow does not make a spring, but I have seen patients who have had several attacks of myocardial infarction and have been in and out of congestive failure for years. This demonstrates the influence of the newer drugs on the immediate prognosis since these patients have had the advantage of mercurials, digitalis, oxygen, etc.

Hypertension has no influence on the immediate prognosis, according to my series. Diabetes decreases the chances of survival, particularly in women. The family history does not seem to be significant in the immediate mortality statistics. When one follows a patient with coronory infarction and sees the tempera-

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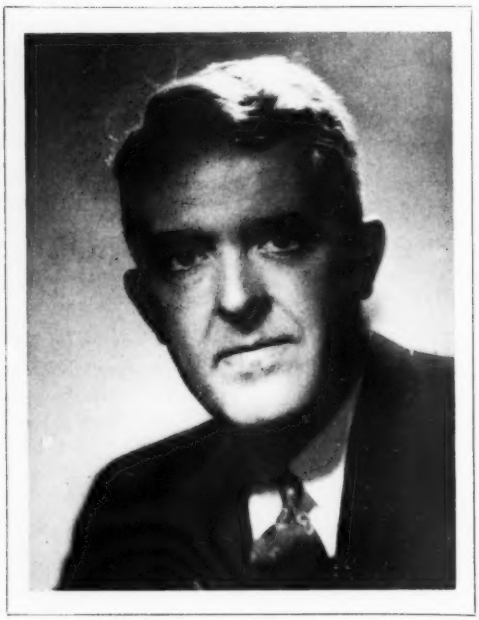
Presented November 2, 1949, before the meeting of the Interstate Postgraduate Medical Association of North America, Philadelphia, Pennsylvania.



WILLIAM G. LEAMAN, JR.

ture climbing each day, one generally looks for a complication in the lung. If a pulmonary complication is absent and the temperature continues to mount, one infers that the infarct is rather large. Therefore, the higher the temperature, as a general rule, the worse the prognosis.

Much can be said about the influence of the pulse rate on prognosis. Pulse rates under 60 or over 110 during these first few critical days are bad prognostic signs, particularly the pulse rates over 110. A fall in blood pressure is more significant in cases in which the blood pressure has been previously normal and here the low pressure, if it persists, is a bad sign.

Obesity, curiously enough, does not seem to be an important factor in acute infarction. The location of the infarct is of no consequence. Cholesterol level, in my opinion, does not influence the outlook in the absence of myxedema.

The routine use of quinidine does not seem to change the mortality statistics. The use of anticoagulants in coronary disease has already been covered for you.[1] As far as I am concerned, I do not think we yet have the ideal anticoagulant. However, the death rate following acute myocardial infarction has been reduced in this country about one-third; the death rate from thromboembolic complications about one-half following routine use of an anticoagulant.

THE next aspect of our subject is the prognosis following healing of the acute myocardial infarction. First of all, the electrocardiographic pattern, viewed as an entity, does not seem to make much difference since patients showing a stabilized pattern, even with persisting evidence of their old, healed lesion, often have as good a prognosis as those whose records have returned to normal. Of more importance is the general trend, as indicated by serial electrocardiograms interpreted in the light of the clinical findings.

Again, heart failure following myocardial infarction increases the gravity of the prognosis although the use of an anticoagulant and a mercurial diuretic will improve the outlook. Should we recommend the prolonged use of the anticoagulant? I do not think so. The patient who takes dicumarol over many months (50 mg. today, 100 tomorrow) I do not think benefits a great deal. This drug will not stem the tide in the chronic case unless the patient is very much in earnest about its use and has the prothrombin time repeated at intervals.

Persisting angina in some chronic cases may actually be beneficial by promoting collateral flow. I wish we had time to go into this aspect a little more completely.

I believe there are few among you who could not study your case records and produce patients showing long survival periods following myocardial infarction. Our first patient this afternoon, Mr. M., a Philadelphian, is 65 years of age and belongs in this category.

In 1932, at the age of 47, he first had an attack of upper substernal pain. For two weeks he had mild transient episodes. A short time later, while sitting quietly in his living room, he had a prolonged seizure lasting a few hours. An electrocardiogram was made the next day by the late Dr. James Talley. For the past 18 years I have followed this patient when I could catch up with him. His electrocardiogram during this time has shown the pattern of an old healed posterior infarction.

Briefly, his family history is negative for heart disease, his blood pressure is normal, his weight has been 118 pounds through the years. Fluoroscopy shows a heart of the ptotic type which is not enlarged. He has few complaints, and

[1]WRIGHT, IRVING S.: Present status of anticoagulant therapy in the treatment of thromboembolic disease. Postgrad. Med. 7:161-5 (March) 1950.

has taken no medication.

Perhaps the patient might like to add a bit to this summary and tell you a few of his experiences through the past 18 years.

PATIENT: I think that following the doctor's instructions to the letter is important. I haven't consulted a physician for any medication or for any sickness for the past 18 years. I have routine studies made once a year. Otherwise, I lead a normal life; I smoke in moderation, seldom use liquor. I do surf casting which requires some physical energy, but I never feel any effects from it. So long as I keep on going as I am, I think that I will be all right.

DR. LEAMAN: How many days have you been ill since your attack?

PATIENT: I have lost three days from my office in 18 years.

DR. LEAMAN: You have then worked 18 years since your infarction. Thank you very much.

This patient has a very good myocardial reserve. He has conquered the fear of heart disease and has continued to work. Now he belongs in a group where the survival rate is comparable to the normal patient of the same age, sex, and race. I want to stress the point that his survival might not have been possible if he had not engaged in normal activities.

OUR next patient, Mr. S., is 47 years of age. He is also a Philadelphian by choice. He came to me for the first cardiac study on January 2, 1941. At that time he was overweight. He has a family history of heart disease; complained of substernal pain which radiated to his left arm after walking one block. His blood pressure was 160/110. He has moderate cardiac enlargement. The electrocardiogram shows a slight depression of the S-T segment in lead 1 and in the precordial leads (CF and V-series).

At the onset I considered the prognosis rather doubtful. The patient was discouraged, used tobacco to excess as well as moderate quantities of alcohol. He kept late hours and was a rather quarrelsome type.

(To the patient): Would you like to tell the Assembly how you overcame a rather difficult situation?

PATIENT: Ten years ago I had a heart attack. There were pains in the upper part of my chest when I walked. They became more frequent and severe so I consulted a neighborhood physician. He told me I had to stop everything, go home and go to bed. I couldn't work and he really did worry me. I went home and sat around waiting for the undertaker. A friend of mine recommended Dr. Leaman. I went to him, although I didn't have much faith in doctors, but he persevered with me and convinced me that if I would live moderately, worry less, and take the medicine he prescribed I could live a normal life. He has proved it in the last 10 years because I feel better now than ever.

DR. LEAMAN: Do you take any medicine, Mr. S.? You said doctors are not much good. What about drugs?

PATIENT: You prescribed nitroglycerin and it helped me. However, one night I had a slight attack and called in a neighborhood doctor, and I told him I was taking nitroglycerin. He said, "Throw that away." I said, "Look, you get out. The medicine helps me." Later, Dr. Leaman told me to continue it if even the slightest upper chest pain appeared. Then I studied the times of the day the pain usually appeared and what caused it and took a tablet under the tongue to prevent it. In this way it does me good.

DR. LEAMAN: I should break in here, I guess. Mr. S., you didn't always do what I told you to do, not by a long sea mile. Remember the time you accepted the job as union representative? I might point out to the Assembly that these patients have been selected from contrasting groups. Mr. M., the first patient, is superintendent of a building. Mr. S. is the representative of a union—the other side of the ticket. I advised him not to engage in activities of that type because of his disposition. These psychosomatic "peeping Toms" have begun to teach me a few lessons and I tried to apply some of these principles with Mr. S. On one occasion, he came back for a routine follow-up examination, the first one in a long time, and told me that he believed he could solve situations as the union representative and continue his work. Wasn't that true?

PATIENT: That is right.

DR. LEAMAN: How did you solve that situation?

PATIENT: After four years of treatment I started to get in pretty good shape. Then I decided to take this job as union steward, and I noticed that I had to take more nitroglycerin tablets than usual, and my blood pressure was reported on the way up again. I found out the boss was the cause of it, so either he had to get out or I had to get out. So I had him fired and the blood pressure went down.

DR. LEAMAN: Thank you, Mr. S. You know, I

often wonder how long the meek will keep this earth after they inherit it. However, I think Mr. S. used his head to save his heart, although I hope the boss didn't have too big a family.

Our last patient, Mr. S., has since cooperated very well and has had a smooth course with few anginal attacks. I think we have one lesson to learn as a result of hearing him outline his experiences. We gave him nitroglycerin to take if he was on the verge of a situation which might be troublesome. He took the drug as a prophylactic measure, and I think through these years he has improved as a result. In his case we encouraged the collateral circulation and I think the prophylactic use of nitroglycerin has proved beneficial. I will leave this thought with you in relation to prognosis. Is mild angina properly managed through the years a beneficial mechanism in producing more collateral flow?

By this time, I think you are beginning to suspect that I am rather optimistic regarding the future of patients who recover from myocardial infarction. I am, under certain conditions, for we can gather abundant clinical evidence to warrant this stand. We know that on the basis of experimental evidence an animal can live with 25 per cent of one kidney, 40 per cent of one lung, 20 per cent of the liver, and 16 per cent of the adrenal cortex. Recently, it has been shown that the heart of the experimental animal continues to beat after 90 per cent of the vessels of the left ventricle have been ligated. Again with only 15 per cent of the myocardium intact the laboratory animal may show no lowering of blood pressure or evidence of congestive failure.

Finally, a word regarding the influence of adequate rehabilitation on prognosis. Cardiac patients can work. I think we have shown that here, and you know it from your own case records. Only yesterday (I speak in terms of a decade or two) their families made invalids of them. Cardiac patients stopped doing everything; they were afraid of working and they were afraid of dying. No attempt was made (for which I blame the specialty known as cardiology) to determine their work capacity.

Today proper physical and psychologic rehabilitation enables the average cardiac patient to pay his own way, to keep his chin up, and to lead a happy, normal life. The cardiac patient must conquer the fear of activity. The first patient here did not bring out that point, but I believe that was his first real achievement. Under conditions that do not require speedy production, the cardiac patient who has mild angina (in the absence of recent infarction) may work without impairing his cardiac reserve. Let us keep that in mind.

I think, in the interests of good prognosis, we cannot tell these patients just simply, "Take it easy, John," and be scientifically accurate. If we do, John will quit his job and may be unemployed for years. Then he may be a real invalid. We must evaluate how much and what kind of work he can do safely. He needs first an adequate medical study which may be termed "cardiac counseling." In large cities the cardiac patient may be referred to the proper rehabilitation bureau where he may discuss the situation with a trained consultant. Here he will learn how he can live within the limits of his disability, but to the maximum of his ability. Finally, we should always remember that the capacity for work depends on the severity of the disease rather than the type of heart disorder.

I think cardiac patients make good employees. In fact, as a group, the cardiac patients will produce at a rate which averages 2 per cent higher than that of unimpaired workers in the same jobs. That is a fact to keep in mind regarding prognosis and the future, and I hope that you will check my remarks with your own office records.

In conclusion, I have summarized some points of importance in formulating the prognosis in coronary heart disease. I have shown 2 patients whose histories illustrate the optimistic outlook: The first has survived an acute infarction for many years on a carefully planned program of living; the second has shown us what can be accomplished in the presence of the anginal syndrome when exciting factors are eliminated and nitroglycerin is used prophylactically.

The value of cardiac counseling and selective placement in industry has been emphasized, and I hope that you will ask your local heart associations if there is a rehabilitation bureau in your city where heart patients may receive this help.

In sketching the optimistic side of coronary heart disease, I always like to quote the remark of the Athenian who was old and quite lame and for these reasons was laughed at by the other soldiers: "I came here to fight," said he, "not to run."

Diagnostic Clinic

Surgical Treatment of Bronchiectasis

GEORGE P. ROSEMOND*

TEMPLE UNIVERSITY SCHOOL OF MEDICINE, PHILADELPHIA

Our experience with bronchiectasis was gained by personal contact with 177 patients on whom 190 resections were done. The discrepancy in number is due to the fact that 9 of these patients had bilateral resections done and 4 of them had two operations done on the same side. The surgery was done by either Dr. W. Emory Burnett or myself.

The diagnosis of bronchiectasis is familiar to you, I am sure. The disease is characterized pathologically by dilatation of the branch bronchi with inflammatory reaction in the area. It is characterized symptomalogically by sputum, which is generally foul, and by blood-spitting. In 81 of our patients there was some evidence of blood-spitting. All had excessive sputum.

To treat these patients definitively it is necessary to consider the etiology of bronchiectasis (Table 1).

TABLE 1

ETIOLOGY OF BRONCHIECTASIS

Unknown	49
Pneumonia	35
Foreign body	17
Sinusitis	15
Post tonsillectomy	13
Lung abscess	12
Empyema	12
Pertussis	10

Of the unknown group, we are quite sure that many had pneumonia as children, and we think quite a few of them had childhood diseases which were accompanied by coughing, especially whooping cough and measles, which give a rather violent type of pneumonia.

TABLE 2

LESS FREQUENT CAUSES OF BRONCHIECTASIS

Post general anesthesia	9
Bronchial stenosis	3
Bronchial adenoma	2
Congenital	2
Inhalation benzene hexachloride	1
Bilateral cases	10

In Table 2 are listed some of the more infrequent causes of bronchiectasis. We are seeing more and more cases due to bronchial adenoma, which, of course, can produce bronchial obstruction to such a degree that bronchiectasis results.

Sinusitis is a very frequent accompaniment of bronchiectasis and was present in 51 of our patients; in 15 of these we thought that sinusitis was certainly a definite etiologic factor although maybe not the entire cause. In 74 patients, however, there was no evidence of sinusitis, or at least there was only minimal sinusitis; the diagnosis in these patients was made by x-ray, so perhaps the nose and throat men would disagree, especially in the relation of bronchiectasis to the minor degrees of sinusitis. There was no record of whether or not sinusitis was present in 65 cases. There is a lot of disagreement as to the exact status of sinusitis as an etiologic factor, but certainly it is very frequently an associated condition.

As to choice of patients for operation, there must be lipiodol evidence of bronchiectasis, and

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Presented October 31, 1949, before the meeting of the Interstate Postgraduate Medical Association of North America, Philadelphia, Pennsylvania.

GEORGE P. ROSEMOND

therefore, before lipiodol bronchography was utilized the diagnosis could not be made and definitive surgery could therefore not be done. The presence of symptoms is necessary and if the symptoms have been present in the past and if the anatomic condition is present, we feel symptoms will return in the future; therefore, it is necessary to operate on these patients.

There must be, of course, limitation of diseased area within the range of possible removal. That means there must be approximately two good lobes left. We can then do a staged resection on two sides, removing, say, the middle and lower lobes on the right side and the lower lobe on the left side and still have enough functioning lung to take care of the individual's needs.

TABLE 3

PREPARATION FOR SURGERY

1. Postural drainage
2. Bronchoscopic aspirations
3. Bacteriology
4. Antibiotics—systemic and aerosol
5. Bronchospirometry
6. Allergy survey if indicated
7. Measures to control oral sepsis
8. Preoperative treatment of sinusitis if present
9. Cardiac survey and overload

The medical treatment for bronchiectasis is outlined in Table 3. Postural drainage is of tremendous importance in preparing a patient for surgery and also in treating a patient medically when he has too much disease to be amenable to surgery. Bronchoscopic aspirations are a marked adjunct to postural drainage. Both are important.

We find that certain bacteria are more susceptible to certain antibiotics and drugs than others, so bacteriology is important.

We utilize bronchospirometry to evaluate the patient's possible response to exercise after surgery is done.

We are realizing more and more the importance of an allergic survey. This is particularly important when we do not know exactly what the etiologic factor is. We find that many of these patients at least have considerable allergic background, and we recently had a patient who is a very good example of possible confusion in diagnosis. This patient did not have saccular bronchiectasis, which we think is an irreversible anatomic situation, but had cylindrical bronchiectasis according to lipiodol x-ray. After proper allergic therapy and elimination of the allergic factor responsible not only did the patient's symptoms subside but the simulated bronchiectasis by x-ray reverted also.

Measures to control oral sepsis are important as far as recontamination is concerned.

We think that both pre- and postoperative treatment of sinusitis is necessary, because certainly if infection is present any place in the respiratory tract it will have its effect at least on the bronchi.

Cardiac survey and overload are done so that we may have a comparison even in a healthy patient should there be any postoperative complication.

THE distribution of pathology in our 190 operations is listed in Table 4. You can see that by far the majority of patients had only a single lobe involved. There is quite a number of segmental lobectomies in this group, and a few pneumonectomies. Two of the patients in this group died on the operating table before any definitive surgery was done.

In the operated cases from 1934 through 1948 the overall mortality before 1942 was rather high (Table 5), and we believe that the reason for this is the fact that about this time we started

TABLE 4
DISTRIBUTION OF PATHOLOGY

	CASES
Single lobe	85
Segment lobe	21
Lobe and segment	44
Multiple lobes	21
One entire lung	17
No resection (patients died on table)	2
TOTAL	190

TABLE 5
OPERATED CASES 1934-1948

	TOTAL CASES	MORTALITY *Number*	MORTALITY *Per Cent*
1934-1941	38	11	29
1942-1948	152	5	3.3
TOTAL	190	16	8.4

doing individual ligation of the bronchi, and also about this time antibiotics were first used. I do not know which is the more important single factor, because we have continued both.

You can see that resection for bronchiectasis is a relatively safe procedure and compares with other major surgical procedures. From 1942 through 1948 there were 5 deaths in 152 operated cases, which included lobectomy and pneumonectomy.

TABLE 6
CORRECTED MORTALITY

	CASES	MORTALITY *Number*	MORTALITY *Per Cent*
Pneumonectomy			
1934-1941	6	2	33
1942-1948	11	2	18
Lobectomy			
1934-1941	32	9	28
1942-1948	141	3	2.1

I do not know whether corrected mortality is a good term, but Table 6 breaks down the mortality and you can see that out of 141 lobectomies, which include segmental lobectomies as well, there were 3 deaths, or 2.1 per cent, which compares with major surgical procedures of other types.

TABLE 7
LIGATION OF BRONCHIAL STUMP

	CASES	EMPYEMA
1934-1941		
Mass	21	18
Individual	17	4
1942-1948		
Mass	2	2
Individual	150	31

There have been empyemas in these cases—too many, I believe (Table 7). I think that we will be able to improve that figure. Empyema is the most common complication that we face following resection.

Figure 1 shows the segmental bronchi of the right lung. This is taken from the work of Jackson and Huber.[1] This anatomic distribution is rather exact, and the various segmental bronchi can be seen on the right. This is lipiodol bronchography demonstrated on a normal patient. The exact anatomic configuration is of tremendous importance when we consider surgery for bronchiectasis, because we like to leave as much lung as possible, of course, and segmental resections have compared, as far as morbidity and mortality are concerned, with the more anatomic complete lobectomies.

Figure 2 shows the same thing on the left side. The distribution is indicated by the lipiodol bronchography. Exact lipiodol bronchography is an absolute prerequisite to the surgery of bronchiectasis.

The basal segments are, of course, more likely to be involved in bronchiectasis.

Figure 3 is an illustration of a patient who does show definite pathology by lipiodol bronchography. This patient is one of the types that we best like to operate on because he had a stricture of his right stem bronchus, probably due to a foreign body. He was known to have swallowed a foreign body as a child. He had very few symptoms for many years, and then developed rather striking symptoms. He expectorated foul sputum in fairly copious quantities; he was underweight and somewhat ill-nourished; he had bouts of pneumonitis almost every year, and he occasionally had blood streaking. Of course, on lipiodol bronchography you can see that his right lower and middle lobes show numerous areas of saccular bronchiectasis and a stricture is clearly shown at the right stem bronchus.

I wish that all lipiodol bronchography was as plain as this. If it is not plain, incidentally, and if we are in doubt after lipiodol bronchography, we repeat at least once. Sometimes we have to wait until medical treatment has been utilized for a period of time to clean up secretions, because if a bronchus is plugged by secretions it is a little difficult to tell what is going on out around the periphery.

[1]Figure 1 and Figure 2 were borrowed from C. L. Jackson, M.D., and J. F. Huber, M.D.

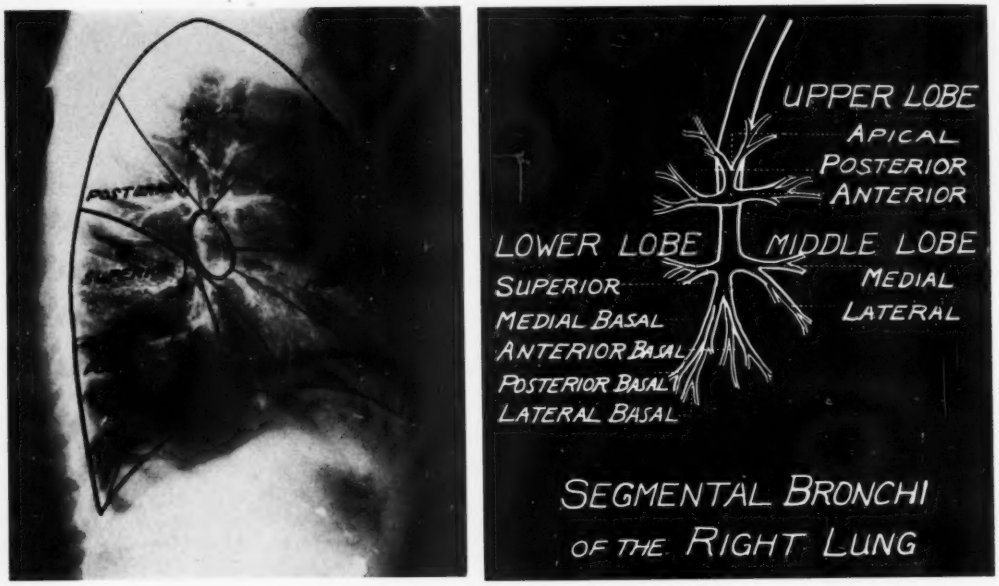


FIGURE 1. Lipiodol bronchography of normal right lung demonstrating segments.

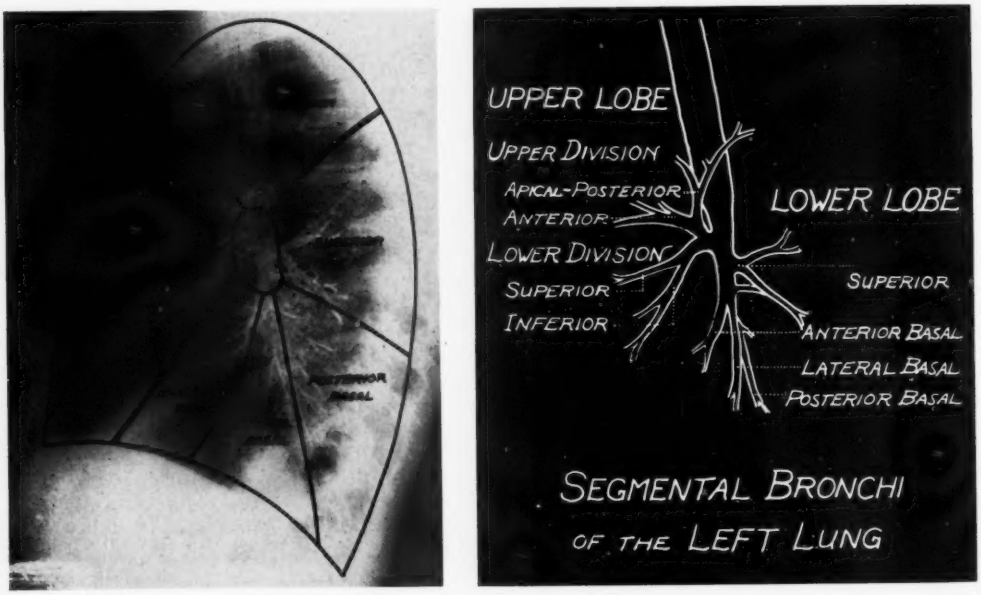


FIGURE 2. Lipiodol bronchography of normal left lung demonstrating segments.

FIGURE 4a is an example of a difficult situation as far as lipiodol bronchography is concerned. This patient had very striking and very marked symptoms. Lipiodol bronchography of his right lung shows that he has a normal right middle lobe and right lower lobe, but there is a

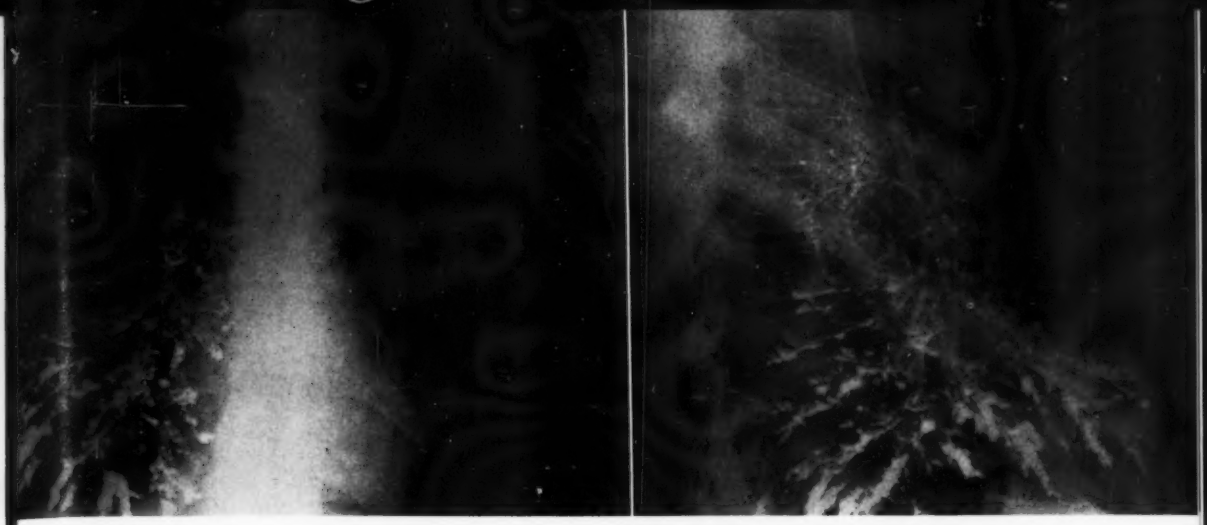


FIGURE 3. Lipiodol bronchography demonstrating saccular bronchiectasis of right middle and lower lobes with stricture of right stem bronchus.

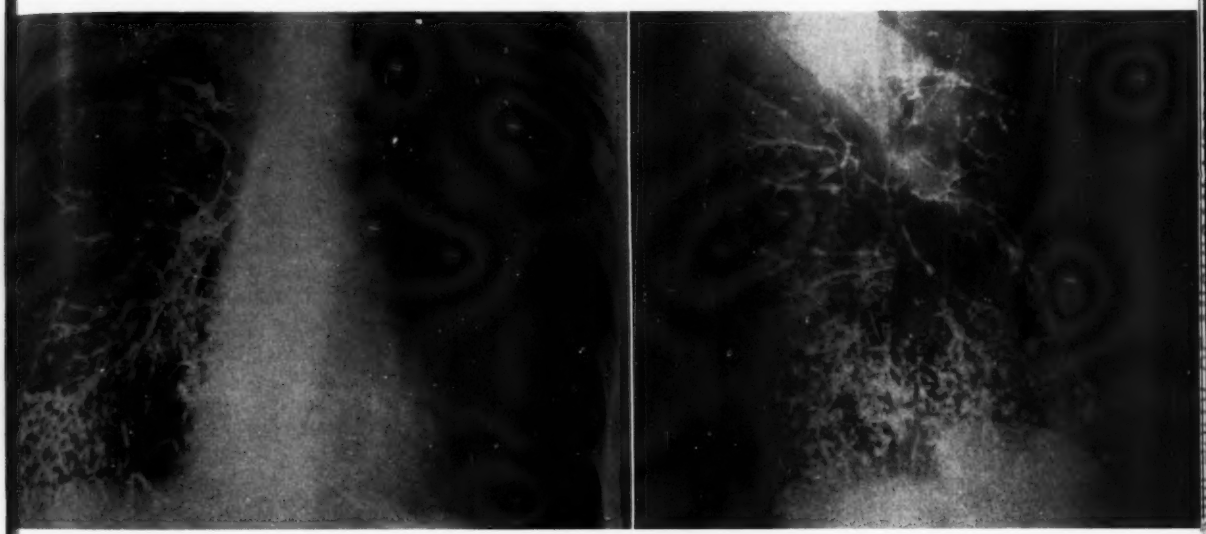


FIGURE 4a. Anteroposterior and lateral bronchography demonstrating normal right middle and lower lobes with diseased right upper lobe.

FIGURE 4b. *(below)* Lipiodol bronchography of left lung demonstrating difficulties in ruling out organic disease in the presence of copious secretions.

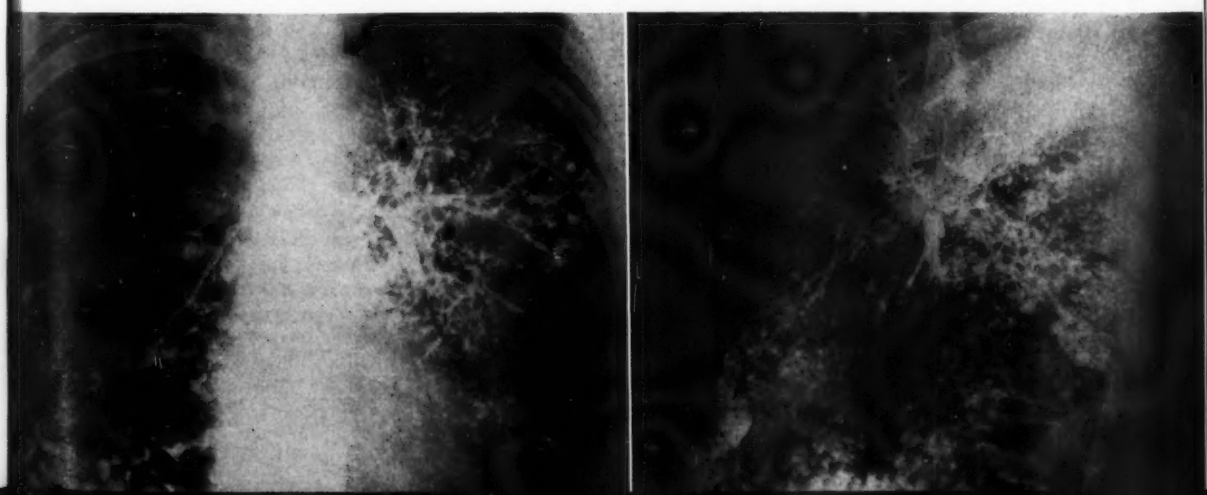


FIGURE 5. Gross specimen demonstrating bronchial obstruction from foreign body, "grass head."

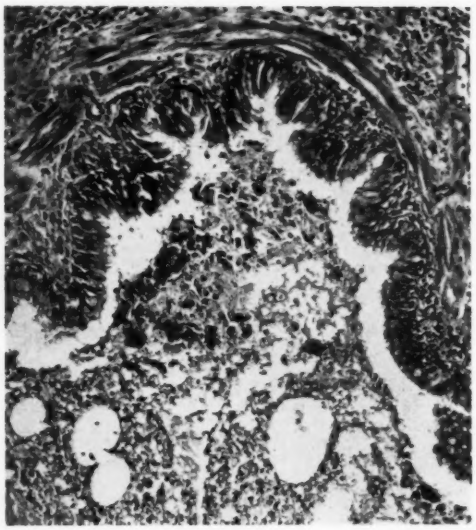


FIGURE 6. High power photomicrograph demonstrating pathologic picture of bronchiectasis.

very fuzzy kind of picture in the upper lobe area and it is a little difficult to evaluate the extent of the bronchiectasis. This patient had very copious quantities of sputum and was almost bled out by repeated hemorrhages from this area. In a patient like this with upper lobe disease we suspect that tuberculosis might be a factor, but we were unable to find any tubercle bacilli in his copious secretions.

Figure 4b is lipiodol bronchography of this patient's opposite side, and again we ran into difficulty. Even after repeating bronchography we were unable to find out what was going on in the left lower lobe because it did not fill completely. You can see the basilar segments are not demonstrated in the left lower lobe. We think that lipiodol bronchography should be done on one side and then after considerable clearing, we map the other side so that we can get a good anteroposterior and a good lateral roentgenogram; we must have exact definitive diagnosis to be able to remove the exact proportion of the lung involved.

We knew that this patient had disease on the right side, and we were a little worried about this left lower lobe. On repeat bronchography, we could not do any better and we assumed that there were two probable reasons for this: (1) maybe he really had disease in this area; (2) maybe his very copious secretion was spilling over here and filling the area.

On bronchoscopy, most of his secretion was found to be coming from the right upper lobe, and so that was a help in diagnosis. All of his bleeding was thought to be, by the bronchoscopist, originating in the right upper lobe, so right upper lobectomy was done and later lipiodol studies of the left lower lobe were perfectly normal.

FIGURE 5 shows an example of a gross specimen. This is the kind of thing we like to find because we can do something about it. This patient had a condition which is very amenable to surgery—localized bronchiectasis due to a foreign body. This is a so-called "grass head." This small child inhaled the "grass head" and had rather striking symptoms for about a year and a half, but the "grass head" remained present during that period of time and when we saw her she had localized bronchiectasis in the left lower lobe. Lobectomy was most successful.

As to the pathology of bronchiectasis mentioned a little bit ago, we expect to find varying degrees of dilatation, thickening due to fibrosis, and chronic granulomatous reaction in the branch bronchi when we remove lobes of lung.

Figure 6 is a high power photomicrograph of lung removed from a patient who was recently operated. You can see the intense inflammatory reaction and the loss of mucous membrane in some areas. Notice the secretion. A very large dilated bronchus can be seen.

Recently we have attempted to follow the patients on whom we have operated during the past fifteen years (Table 8). In 190 operations, including 13 bilateral two-staged lobectomies, there were 18 deaths, most of which were in the early group; 137 patients have been followed for one to fifteen years; we have as yet been unable to obtain a definite follow-up on 22 patients. Of the 137 patients, 92 are relatively asymptomatic, and 33 have mild symptoms, such as slight cough with expectoration and sometimes blood spitting, which is rather slight in degree. We consider that this combined figure represents a fairly good result. There are moderate symptoms in 9 patients and severe symptoms in 3 patients. We consider that 9 per cent constituted poor results. We did not gain anything on the ones with moderate symptoms; they had moderate symptoms before operation and still have them. The 3 with severe symptoms believe they became worse after operation.

TABLE 8

RESULTS IN 137 PATIENTS FOLLOWED 1 TO 15 YEARS

	NUMBER	PER CENT
Asymptomatic	92	67
Mild symptoms	33	24
Moderate symptoms	9	7
Severe symptoms	3	2

I AM afraid that we have not always chosen these patients quite as properly as we should. We believe that by choosing them properly we can increase the good results to almost 100 per cent. The patients that give us the best results, of course, have local lesions produced by a known etiologic agent a long time ago, a foreign body, for example, and we expect 100 per cent good results in that type of patient. If a patient has localized symptoms and the etiology also occurred many years ago but with something like a pneumonitis and when there have been no repeated episodes, we expect 100 per cent improvement. If a patient is very much under par and we are unable to improve him by medical measures; if the disease is fairly widespread and maybe questionably out of bounds; if there have been recurring episodes of respiratory infection and especially if there may be some factor such as an allergy which is difficult to avoid in the future, or if there is marked sinusitis, we are a little bit more cagey in our prognosis, and we cannot be quite so sure. Of course, sinusitis must be followed constantly. We have had a patient back in the hospital recently who was again beginning to get symptoms which certainly simulated bronchiectasis because of neglected sinusitis. Postoperative care of possible etiologic factors should not be neglected.

We have with us today a patient who is an illustrative case because she has had a bilateral segmental lobectomy done. She illustrates several points. One is her etiology. She had both whooping cough and measles when she was about 9 years of age, and has never been entirely well since. She has had recurring episodes of pneumonitis. She has had sputum which is moderately copious, at least which was copious, and which was also odorous on occasion to the extent that she was a little bit worried about getting out in a gathering with other people. When she came to us, she had positive x-ray findings.

Figure 7 is lipiodol bronchography of her right side. This is rather good lipiodol bronchography, as we expect it to be. If it were not that good we would certainly resort to medical measures for a short time to try to clear up the secretion so we could fill the bronchi better. You can see the disease in the basal segments of the right lower lobe. The right upper lobe and the right middle lobe are entirely normal.

After a week or ten days, the opposite side could be lipiodoled; again, there was an almost equal distribution of the disease in the basilar segments of the left lower lobe. Notice in Figure 8 how they stand out on the lateral x-ray. The lateral is quite necessary to determine the extent of the disease. We often use oblique x-rays when we are not quite sure about the exact extent of disease.

Figure 9 shows the left side five days after a segmental lobectomy was done. The superior segment of the left lower lobe was left intact, that showing no disease at all; the basal segments were removed. This x-ray shows the resected rib, which is the sixth. We do not like to operate these patients just after lipiodol bronchography because pulmonary functional studies do not return to normal for from three to five days, and we are sure they retain lipiodol for a

FIGURE 7. Lipiodol bronchography on right side demonstrating bronchiectasis in basal segments of right lower lobe.

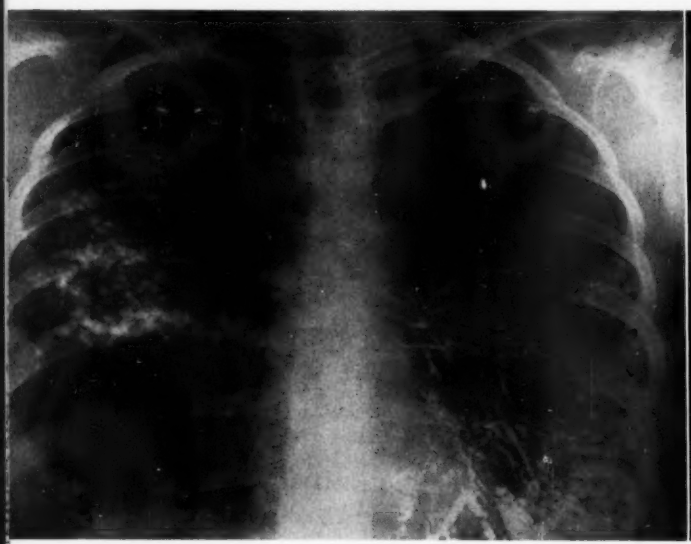
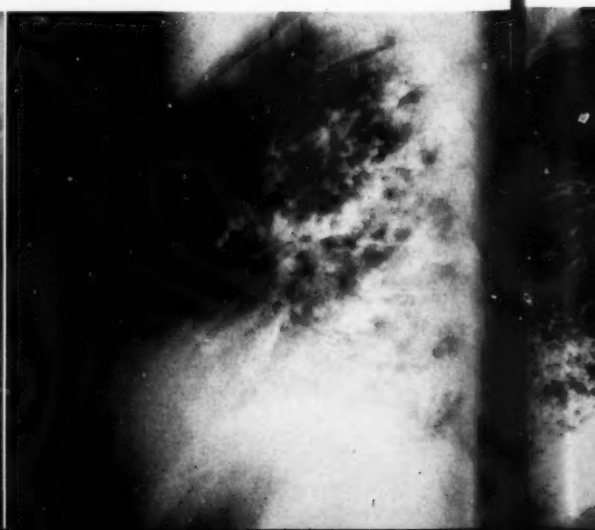


FIGURE 8. Lipiodol bronchography of left lung demonstrating bronchiectasis of basilar segments of left lower lobe.

FIGURE 9. *(below)* Roentgenogram five days after resection of basilar segments of left lower lobe.



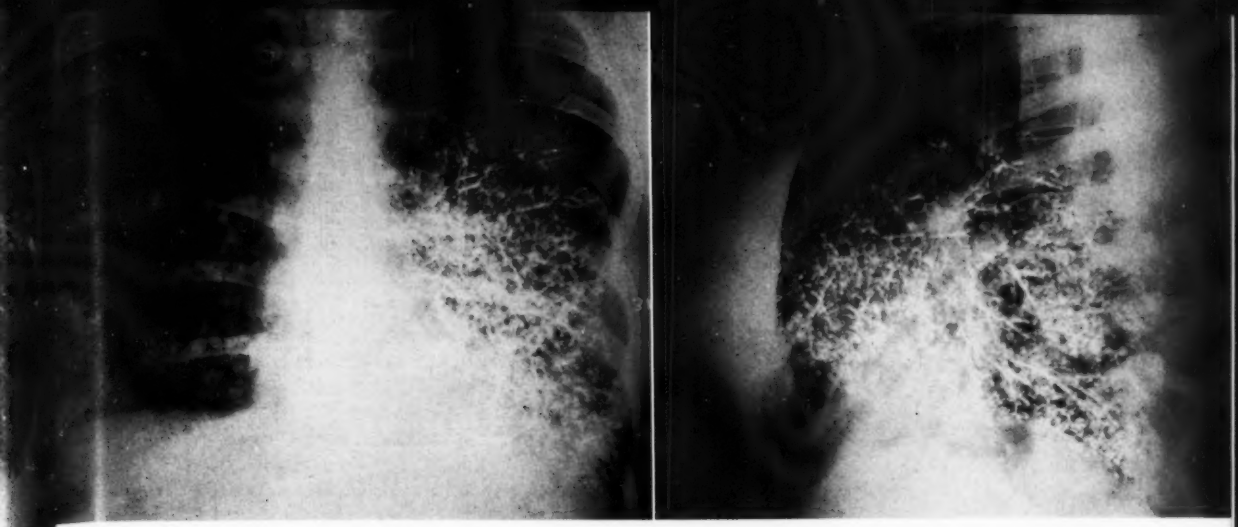


FIGURE 10. Lipiodol bronchography on left side after resection of left lower lobe basilar segments.

FIGURE 11. Roentgenogram five days after resection of basilar segments of right lower lobe.

FIGURE 12. *(below)* Lipiodol bronchography two months after resection of basilar segments of right lower lobe.

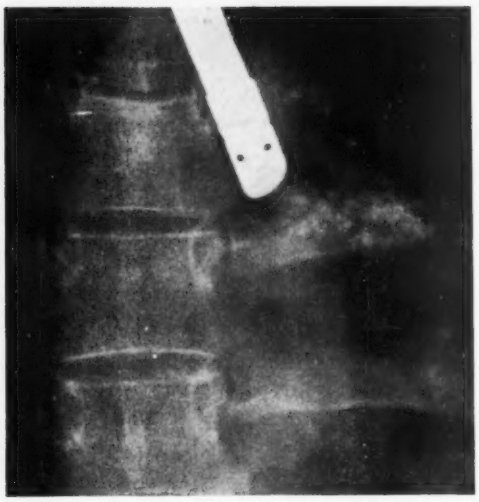


FIGURE 13. Bronchospirometry catheter in position in left main bronchus.

much longer period. We prefer to wait two weeks, and some surgeons like to wait a little longer. We prefer to wait until the x-ray findings are entirely cleared up, but that takes too long. Ordinarily we wait at least two weeks.

We were not quite sure of the mapping on the right side because it contained secretions, so we remapped here between stages. The mapping on the right side has been repeated, showing again about the same distribution of bronchiectasis as previously demonstrated.

Another mapping was done on the left side showing that the resected area is now entirely normal (Figure 10). We are unable to find any evidence of bronchiectasis here, even though the superior segment of the left lower lobe was left intact. We have these lipiodols repeated one month before going on with the second stage, and we prefer at least that much interval.

Her second stage was done one year after the first stage. We do not believe there is any great hurry, provided the patient is not having numerous acute episodes, in staging these operations. We prefer the patient to get back entirely to normal, which we feel she does after a year. Sometimes six months is sufficient. It takes several months to recover entirely from lobectomy; it takes at least three months for pulmonary function studies to return to a stable situation.

Figure 11 was made after the second stage procedure, the right segmental lobectomy. You can see a tube in place for drainage. Sometimes we utilize these tubes; sometimes we do not. This is a matter of choice.

LIPIODOL studies after the second stage procedure are shown in Figure 12. There are very tiny areas of mild cylindrical bronchiectasis in the remaining segments of the lung, which illustrate the slight chance of inaccuracy in doing segmental lobectomy, but that is a relatively normal right side with the superior segment left intact and segmental lobectomy on both sides completed.

Figure 13 shows the bronchospirometer tube in place in the left main bronchus.

There is no particular limitation of motion. These incisions are fairly symmetrical. They would show in a two-piece bathing suit.

The operation was done through the sixth rib bed, that rib having been removed. Her function has returned entirely to normal and she is relatively asymptomatic. We still have to check her sinuses from time to time, which is being done by a nose and throat consultant.

In conclusion, I would like to say that if a patient is thoroughly studied and if there are definite indications for lobectomy, and they have been presented to you, surgery for bronchiectasis need not be feared and is the curative method of treatment.

COMING POSTGRADUATE COURSES

The Tulane University of Louisiana School of Medicine, New Orleans

Therapeutics as applied to general practice, November 6-10, Dr. R. L. Pullen, chairman

Electrocardiography, November 27-December 8, Dr. George E. Burch, chairman

Recent advances in internal medicine, March 12-17, Drs. J. Robert Snavely and Roy Turner, chairmen

Obstetrics, April 2-7, Dr. Isadore Dyer, chairman

The specialties as applied to general practice, April 9-14, Dr. R. L. Pullen, chairman

Psychiatry and neurology, June 18-23, Dr. Robert Heath, chairman

Cardiology (newly designed course), February 19-March 2, Dr. George Burch, chairman

Diagnostic Clinic

The Ulcer Problem

ISIDOR S. RAVDIN*

UNIVERSITY OF PENNSYLVANIA SCHOOL OF MEDICINE, PHILADELPHIA

MANY of the problems of gastric and duodenal ulcer have been reviewed so often that it would seem that they should have been finally settled years ago; and yet perennially the subject is reopened with renewed vigor and with little or no more unanimity of opinion than existed a decade or more ago. Internists all too frequently do not agree with other internists, or surgeons with other surgeons, while the two groups frequently hold widely divergent opinions.

There has always been some doubt as to whether gastric and duodenal ulcers have a common primary etiology. It is indeed possible that the so-called primary etiologic factors may be of purely secondary importance. That free hydrochloric acid in the gastric secretion plays an important part in the failure of an ulcer to heal can hardly be questioned, but that it is the motivating factor in the initiation of the ulcer *is* open to serious question. The volume and the hydrochloric acid content of the gastric secretion, especially the nocturnal secretion, in patients with duodenal ulcer, are increased. They are usually not so high in patients with gastric ulcer; in fact the average volume of gastric juice is approximately the same as for normal subjects and the hydrochloric acid content is often lower than that of normal subjects.

*From the Harrison Department of Surgical Research, Schools of Medicine, University of Pennsylvania, and the Department of Surgery, Hospital of the University of Pennsylvania, Philadelphia, Pennsylvania.

Presented October 31, 1949, before the meeting of the Interstate Postgraduate Medical Association of North America, Philadelphia, Pennsylvania.

THE GASTRIC ULCER

It would be of the greatest importance were we able to agree on whether a benign gastric ulcer ever becomes malignant. From a review of the literature it would seem that this is not now possible. I believe that a benign gastric ulcer can become malignant. I am fortified in this opinion by a number of circumstances which seem to me beyond serious doubt. Chronic ulceration of mucous surfaces in other locations is known to undergo malignant change. This is generally agreed to in the oropharynx, and the large bowel, which are otherwise common sites for malignant tumors.

We have on occasion seen roentgenologic studies of supposedly benign gastric ulcers made at intervals over years and finally at the same area carcinoma makes its appearance. I am convinced that a benign ulcer can become the site of malignant change. Early carcinoma is often present in a benign ulcer known to be present for some years.

The importance of obtaining greater unanimity of opinion on this subject should immediately become evident, for if a benign gastric ulcer can become a malignant gastric lesion, every patient with a gastric ulcer should be subjected to early operation.

It will be generally agreed that it is at times impossible for even the most skillful roentgenologist to distinguish between a benign and a malignant gastric ulcer. The size of the ulcer is of little help. The position of the ulcer is of only limited help except for ulcers of the greater curvature, all of which should be considered

malignant from their inception. Even roentgenologic evidence of supposed healing as evidenced by filling of the defect cannot be accepted as bona fide evidence of healing, for in the most unsuspecting instances such a circumstance may be associated with actively growing cells filling the previously demonstrated crater.

Nor can any other laboratory aid assist materially in the differential diagnosis. The gastric acid curves are of limited value. The nocturnal gastric secretion in patients with gastric cancer is usually less than in patients with gastric ulcer, and may be less than that of normal subjects, but there are many exceptions to this generalization. The study of the gastric potential is helpful but not finally diagnostic. The Huggins iodoacetate and the Seibert polysaccharide tests are informative but at this time hardly more than that. In the hands of Dr. Papanicolaou and his associates the study of exfoliated cells obtained from gastric washings has become helpful, but in the hands of others with less experience and exacting technic the method is not sufficiently diagnostic to place too great reliance upon it.

Gastroscopy in the hands of experts is helpful, but I have had so many failures to diagnose a malignant lesion which should have been seen that I have all but given up this method of diagnosis. If the truth were told the surgeon at times is unable even with the stomach in his hands to tell with accuracy whether the lesion is benign or malignant. Except for the lesions along the greater curvature, the position of the ulcer often cannot create more than a suspicion of its character. Prepyloric lesions are frequently benign, but it should be noted that the prepyloric malignancies frequently offer the best chance of a five-year cure. Perhaps this is due to earlier symptoms requiring operation and thus a better chance for cure. It is certain that in this location a more extensive resection is usually possible.

I myself have become firmly convinced that the way to improve our present poor end results in the surgery of gastric cancer is to treat surgically what may be or may become a cancerous lesion. This method is used in the thyroid, the mouth, the breast, the large bowel, and many other sites. Why we should be so reticent with lesions of the stomach is difficult to explain. In my own hospital internists and surgeons have agreed that therapy for a supposed gastric ulcer shall not exceed five weeks after which any roentgenologic evidence of persistence of the ulcer is indication for operation.

HEMORRHAGE

There can be little question that hemorrhage is the commonest of the major complications of ulcer. It occurs in the duodenal ulcer more frequently than in the gastric ulcer. Many patients have had a history of previous hemorrhage.

While the indications for operation in perforation are clear, the indications for operation in the presence of hemorrhage are not so clear. Stewart has recently advocated radical resection for patients who have bled grossly into the upper gastrointestinal tract within one week of admission; where the admission red cell count was 2.5 million per cubic millimeter or less, and the total circulating red cell mass was 60 per cent or less of normal and there is reasonably good evidence for the clinical diagnosis of ulcer.

This technic has been carried out by Stewart with increasing success, so that in the last 33 consecutive resections in such acutely exsanguinated patients there has been but 1 death. Dr. Stewart points out the operation which is done under such circumstances, subtotal gastrectomy, is the same as that done under less critical circumstances. The patient therefore not only obtains relief from the risk of hemorrhage, but cure of the ulcer.

While I must admit to agreeing with Dr. Stewart from a philosophic point of view, I cannot bring myself to the point of intellectually agreeing with him that every patient with severe hemorrhage from a probable ulcer should be subjected to immediate gastric resection. Such a concept accepts no other plan than resection.

In the Hospital of the University of Pennsylvania where internists and surgeons have long been interested in this subject the data point strongly to the fact that when all bleeding ulcers are considered, a controlled medical program is associated with the lowest mortality. T. Grier Miller has found the mortality following the use of a Meulengracht or similar diet to be 2 per cent in a series of over 300 patients. The difficulty with many of the reported series treated by internists is that they do not include the deaths which occur when, as the result of failure of a medical program, patients are transferred for operation following several days of exsanguinating hemorrhage during which time hypotension and anoxia have persisted. The surgical mortality under such circumstances approximates 100 per cent.

We are now following a plan which can be summarized as follows:

1. Since the exsanguinating hemorrhages nearly always occur from the posterior duodenal wall ulcers, if it is known that the patient has such an ulcer, operation is resorted to as soon as it is determined that continuing hemorrhage places the life of the patient in great jeopardy.

2. The older the patient the greater the likelihood of surgical therapy being necessary, for older patients with less elastic vascular systems stand hemorrhage more poorly.

3. A history of previous hemorrhages should be considered as a clear indication for operation although this may not be necessary in the emergency itself.

Whether the operation is done as an emergency or after cessation of the bleeding and partial recovery from the anemia, the operation for a bleeding ulcer should, in my opinion, consist of a radical gastrectomy with resection of the ulcer. Dependence must not be placed upon vagus resection. Gastroenterostomy, with or without attempted external ligation of vessels around the site of the ulcer, is useless. In a bleeding duodenal ulcer requiring operation, radical gastrectomy, without simultaneous excision of the ulcer site, is only rarely justifiable. Only radical gastrectomy and duodenectomy of the ulcer area as recommended by Roscoe Graham should be done for bleeding duodenal ulcers requiring surgical therapy. Properly planned and executed, with blood transfusions before, during, and after operation, the risk is indeed small as Stewart has shown. Very occasionally the ulcer must be left behind, but it is then handled as suggested by Graham.

Let me repeat again, the mortality of a well-planned and executed medical and surgical program should not exceed 5 per cent. If minor operations are done the mortality will be high, even if operation is done reasonably early—26 per cent in our hospital. If a radical resection is done early, the mortality will be low—8 per cent in our series; and if done late, when irreversible shock has supervened, it will be high—100 per cent in our series. It is important, therefore, that each patient be seen frequently by both internist and surgeon and that they share the responsibility and pool their experience, judgment, and therapeutic resources.

PERFORATION

There can hardly be any doubt that the clearest indication for operation is the perforated ulcer. In 1940 DeBakey and Odom stated "There is probably no other complication of gastroduodenal ulceration that requires more serious consideration than acute perforation. This is evinced by the apparent increase in its incidence and the general mortality of approximately 25 per cent." DeBakey and Odom stated that "of even greater interest is the fact that during the past decade (1930-1940) the general mortality in acute perforated gastroduodenal ulceration has not materially decreased." During the past decade there has been a very material reduction in the general operative mortality of these lesions. The mortality in the Hospital of the University of Pennsylvania during the four-year period being reported on was 2.4 per cent and in the last 39 consecutive cases of perforated ulcer there has not been a single death.

Seely's method of using gastric suction drainage and chemotherapy in the nonsurgical therapy of perforation is not new, although he has had a wider experience with it than any other surgeon. Rhoads and Nagel and I used this method and reported its use in 1938. Seely states that the patient should not have eaten shortly before perforation, and the patient should be seen, and therapy initiated, very early after perforation. This is a method which if widely used will, I am afraid, lead to an increased mortality, for Seely's rigid criteria may be ignored.

The duty of the physician and surgeon following diagnosis of perforation is clear, for the most important consideration is the saving of the life of the patient. If the history is a good one and if the physical signs are positive, the surgeon need not wait for the demonstration by roentgen ray study of air under the diaphragm. Exploratory laparotomy with simple suture of the perforation and reinforcement with omentum is at present the classical therapy. Gastric resection, although extensively used by some surgeons, in the presence even of a simple chemical peritonitis, is, I believe, not advisable.

Gastric suction drainage should be established as soon as the perforation is closed. Under such therapy edema at the perforation site rapidly disappears and gastrointestinal continuity is shortly re-established.

The mortality after free perforation is generally still too high. Peritonitis offers a threat of major importance to life, and the longer the

time from perforation to operation the higher will be the mortality with any method of therapy.

Perforation, contrary to general opinion, does not always lead to permanent healing of the ulcer. More than 50 per cent of such patients operated on by us continued to have serious complaints requiring later resection. If symptoms continue, subsequent therapy should be based on the merits of the individual case. Although bilateral infradiaphragmatic vagotomy at the time of closure of the perforation might reduce the need of later operation, it is believed that even this procedure is inadvisable since it would increase the period of gastric retention.

INTRACTABILITY TO MEDICAL THERAPY

Failure to obtain healing in a duodenal ulcer after a good medical program, the persistence of symptoms, especially pain, and the evidences of penetration are indications for surgical therapy. If an adequate diet has been maintained for a reasonable period, if smoking has been stopped, and mental stress and strain relieved, and if, in spite of these, the symptoms persist, surgical therapy is the only means worth trying. Protein hydrolysates, in our experience, have little to offer over a well-planned and administered diet. They are no cure-all for gastric or duodenal ulceration.

However, radical gastric resection or vagotomy should not be done merely because the patient refuses to follow, or fails to live within, the careful requirements of a well constituted medical program.

PYLORIC OBSTRUCTION

Pyloric obstruction, either from a gastric ulcer in the pylorus or a duodenal ulcer, is not uncommon. Frequently the obstruction is not due to cicatricial stenosis but is associated with spasm or edema or both. When the obstruction is the result of pyloric spasm it is relieved, in whole or in part, by the administration of spasmolytic agents. When due to edema, with or without coincidental spasm, the differential diagnosis, even with the aid of competent roentgenologic study, may be difficult. The existence of a low plasma protein is suggestive that the obstruction is due at least in part to edema. Under such circumstances the institution of suction drainage, which puts the stomach at rest, and the administration of plasma or albumin infusion, will result after a few days in definite evidence of a functioning pylorus.

The chronically obstructed ulcer patient is frequently malnourished. This is often due in part to the rigid diet which medical practitioners have previously imposed on these patients; in part to a restriction in food intake by the patient because of pain; and in part to the vomiting of food ingested. Thus, many of the obstructed patients come for relief with obvious evidences of dehydration and salt loss. Attempts to correct the dehydration and salt loss by the administration of sodium chloride often serve only to intensify the edema.

It should have been equally obvious to us that these patients may also have deficits in various vitamins, especially vitamin C and the B complex; that they may have had not only a serious depletion of the plasma protein, but also a moderate or severe reduction of the plasma and blood volume. The preparation of these patients prior to operation is, therefore, of the greatest importance if morbidity and mortality are to be kept as low as possible.

OPERATIVE THERAPY

I HAVE already indicated that the only operation which can be considered adequate for a gastric ulcer is a radical gastrectomy. Local excision, pyloric resection, or even vagotomy have, we believe, no place in the therapy of a lesion which, if not already malignant, may provide the fertile soil for subsequent neoplastic change. The decision should not rest on the opinion of the internist, the radiologist, or the gastroscopist —nor even the surgeon with the abdomen open and the offending lesion in his hand.

The best radiologists frequently indicate their inability to distinguish between a benign and a malignant lesion. The internist all too frequently fails to realize that persistence of even minor symptoms may be a dangerous omen; and the gastroscopist has in our experience too often been of little help in the very patients for whom we need help most. Only the microscopist is of real help after study of the entire ulcer area.

If this be true, and I am sure that it is, a radical resection remains the operation of choice. The experience of more than a decade is now sufficient to assure us that this operation is attended by a high incidence of cure, by a low incidence of recurrence of ulceration, either in the stomach or jejunum (4 per cent), and by a low mortality.

In the ulcers of the cardia the operation of choice is a transthoracic transdiaphragmatic gastric resection. We have in 2 instances done total gastrectomies for lesions that eventually proved to be benign ulcerations.

Whatever the approach and whatever the operation the resection should be adequate and by this I mean that not less than 70 per cent of the stomach should be resected. It is just as easy to do a major resection as a minor one, and it is no more difficult to do the anastomosis necessary for the restoration of gastrointestinal continuity. One must at the operating table measure the extent of the proposed resection. It is often impossible to tell how much was resected by weighing the excised portion of the stomach.

In duodenal ulcer the operation should be of similar extent if the patient is to obtain the best possible postoperative result. In the gastric ulcerations in the prepyloric area it is safer to excise 2 cm. of the duodenum, for should the lesion prove to be malignant, subsequent metastasis may take place from a postpyloric extension of the tumor and not from preoperative lymphatic spread of the tumor.

In every instance of duodenal ulcer where it is possible the ulcer site should be excised. By careful dissection this can be done more frequently than is now being done. At times the duodenal ulcer cannot be safely resected, but such instances are not common. When this does occur, a radical gastrectomy can still be done. The important technical step under such circumstances is that no pyloric gastric mucosa be left behind. Even though it becomes necessary to transect the pylorus, all gastric mucosa should be carefully separated from the submucosa and excised before closing the pyloric stump.

In resection for bleeding ulcer, the ulcer should, if at all possible, be excised. If the operation is done during acute hemorrhage, resection of the ulcer area is nearly mandatory. Dependence upon the extent of the gastric resection and ligation of periduodenal vessels is an ill-conceived and dangerous procedure.

Satisfactory closure of the duodenal stump is the most important technical aspect of the operation when the Billroth II principle is used. While in certain instances the Billroth I principle can be utilized, experience abroad and in this country strongly favors the Billroth II procedure. The restoration of gastrointestinal continuity can be accomplished by numerous variations of this general principle. The value of the Hofmeister procedure of carrying the resection high on the lesser gastric curvature, with closure of the medial aspect of the gastric stump and anastomosis of the stump adjacent to the greater curvature, remains the method of choice of most surgeons with a sustained interest in this field of surgery.

If two-thirds or preferably more of the stomach is removed, including all gastric mucosa at the pyloric outlet; if the ulcer is excised whenever possible; if a short jejunal loop is anastomosed to the gastric stump, either by the antecolic or retrocolic method; and if the duodenal stump is mobilized freely so as to provide for adequate closure, intra-abdominal postoperative complications are rare, and recurrent and marginal ulcer in the later period, uncommon.

I prefer the antecolic type of anastomosis even in the obese patient. Resection of 75 to 80 per cent of the stomach has increased the incidence of the dumping syndrome over that occurring following a less extensive resection.

It is important not to turn in too much of the stomach or jejunum at the site of anastomosis for this prolongs the period of gastric retention following operation. The administration of postoperative fluids should be based upon what the patient needs and only that. The decreased urinary output so frequently observed in these patients immediately after operation is associated with a decrease in the gastric pouch output, a retention of sodium and chloride, and an excess excretion of potassium. The picture is that seen in increased adrenal cortical activity. The administration at this time of large amounts of sodium chloride will further accentuate the edema of trauma.

The indwelling gastric tube is usually removed forty-eight hours after operation. The patients are out of bed and walking twenty-four hours after operation and the diet is rapidly increased following removal of the Levine tube. In five or six days they are usually on a six-meal-a-day low residue diet and they leave the hospital in an average of eleven days. Within four to six months they are taking a three-meal diet without any major restrictions.

The major complication of this operation in our experience has been postoperative atelectasis. The resident staff must be constantly aware of the likelihood of this complication and encour-

age bronchial evacuation. Should intense right upper abdominal or epigastric pain occur from the fourth to the seventh day, leakage from the duodenal stump should be presumed. If this seems likely an incision is made without delay and a sump drain is inserted under the liver edge toward the duodenal stump. We have had this complication occur three times in this series of patients. In the first instance the patient rapidly improved and was later discharged from the hospital only to return a month later with a subdiaphragmatic abscess; in the remaining 2 the immediate institution of sump drainage resulted in early recovery.

We have had few postoperative sequelae other than the above except for the "dumping syndrome." It has occurred in some form in about 15 per cent of our patients, an incidence slightly higher than reported by other surgeons. We believe this is the expected incidence when all patients are closely questioned. It is usually of brief duration and only in exceptional circumstances annoys the patient for more than three or four months. It is due, we believe—following the studies of Machella—to the passage of high concentrations of digested foodstuffs into the jejunum causing jejunal distention, for this is a portion of the bowel normally accustomed to receiving hydrolysates at or below that of isotonicity.

You will wonder why I have not said more regarding vagotomy. This operation, revived and elaborated so beautifully by Dr. Dragstedt, provides a physiologic approach to certain of the factors associated perhaps with the initiation of the ulcer and certainly with its chronicity. Bilateral vagotomy reduces gastric secretion and the hydrochloric acid content of this secretion. It relieves pain and provides a chemical condition more conducive to healing. It is, however, associated with a high incidence of postoperative gastric retention which occasionally becomes alarming, and in at least 75 per cent of our patients has been, to say the least, most annoying. To perform a vagotomy and a posterior gastroenterostomy is as time-consuming as a radical resection and far less satisfactory.

A "complete" vagotomy, as judged by a carefully done insulin test, in patients with duodenal ulcer, is followed by gastric retention. The retention may give rise to troublesome symptoms for from two to twelve months. This can be corrected or prevented by another operation, gastroenterostomy, or pharmacologically by the use of such drugs as urecholine or doryl. Such a result does not permit the prompt return of the patient to a useful way of life.

Vagotomy has given satisfactory results in patients with marginal or jejunal ulcer, especially if a thorough vagus resection is done.

An incomplete vagotomy, which may follow even the most careful dissection, plus a gastroenterostomy, may be followed by a marginal ulcer or by a failure of the duodenal ulcer to heal.

Vagotomy is already being used as a means of reducing the extent of the gastric resection. We believe this to be an unwise procedure.

To obtain a good result from an adequate gastric resection one does not require vagotomy.

A NUMBER of thousands of ulcer patients have now been partially or completely vagotomized at a level just above or below the diaphragm. There are available data on these patients, and at least one group is collecting these at the national level. We now know that division of the vagi above the stomach provides immediate relief from pain. It does, however, superimpose a condition of delayed gastric emptying in most patients and, in some instances, one of massive gastric retention. In others, an intractable diarrhea results.

Gastric retention, the belching of foul-smelling gastric contents, and a persistent feeling of fullness, which so many of our patients have had, are unphysiologic conditions which have resulted from a physiologic approach to the ulcer problem.

The objective of any operation for ulcer should be to remove the ulcer and to obtain a permanent reduction in free hydrochloric acid secretion. In no other way can surgery offer, at present, a high percentage of cures.

The surgeon who is considering operation for a gastric or duodenal ulcer must, as Roscoe Graham has so well said, "take into consideration (1) the site of the ulcer; (2) the character of the pathologic lesion; (3) the associated physiologic disturbances; (4) the resultant biochemical disturbances; (5) the age of the patient." When the patient accepts the decision that surgical therapy offers the best chance for cure, he should expect (1) an excellent chance of recovery from the operation; (2) relief from symptoms; (3) reasonable assurance against recurrence, and (4) ability to return to work.

Uses of Pentobarbital Intravenously

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THE purpose of this paper is to bring to the attention of the practicing physician a simple, successful method of complementing conduction anesthesia (topical, infiltration, regional, peridural, or spinal) by employing a time tested drug—pentobarbital (nembutal*) intravenously. Packaged as a stable liquid, it is useful whenever instant hypnosis for control of nervousness or actual convulsions is needed by the physician in the home, office, or hospital.

HISTORY

Fitch, Waters, and Tatum[1] were among the first (1930) investigators to report their findings with intravenous pentobarbital. During the twenty years since that report relatively few papers[1-11] on the intravenous use of this drug have appeared in the literature. In spite of this fact, pentobarbital intravenously is widely used by anesthesiologists today.

Rowbotham[2] reported in 1931 the use of pentobarbital intravenously as an ideal method to produce unconsciousness for the patient in his own bed so that he might be spared the psychic trauma of consciously being moved to the operating room. While it would not be practical to apply this routinely, there are certain types of surgical problems such as toxic thyroid patients who should be handled in this way. His report was made before the advent of pentothal, but even so it is our opinion that for induction in bed, pentobarbital offers the advantages of being (1) longer acting, (2) less likely to cause laryngospasm, as well as (3) less respiratory depressing in a sleep dose, therefore safer than pentothal for that purpose.

Magill[3] and Ashworth[7] reported the use intravenously of pentobarbital as induction preceding inhalation anesthesia. They mentioned the advantages of the intravenous route over the rectal or oral route in determining an accurate dose—also the fact that premedication need be started only ten minutes prior to surgery.

Abbott[4] and Campion[8] reported the use of intravenous pentobarbital during labor, stating that it is a safe and effective hypnotic in the control of labor pains, that hospitalization is necessary, and that restlessness is a disadvantage requiring special nursing care. No detrimental effect on the infant, such as respiratory depression, was seen. Volpitto[10] reported for obstetric amnesia the use of pentobarbital and scopolamine hydrobromide in sterile distilled water in the proportion of 0.025 gm. (3/8 gr.) of pentobarbital and 0.00064 gm. (1/100 gr.) of scopolamine per cubic centimeter. The average patient required about 10 cc. of this mixture to produce amnesia—not analgesia or anesthesia.

Wright[5] successfully used pentobarbital intravenously to control ether convulsions. Ross[6] advocated the use of pentobarbital intravenously for the control of convulsions in eclampsia. Carron[11] described the use of pentobarbital intravenously with curare for endotracheal intubation. He named as its advantages that it is less likely to initiate laryngospasm than is pentothal—also the dose of pentothal required to provide adequate anesthesia for intubation is frequently excessive and may cause respiratory

*Pentobarbital (Nembutal), supplied by Abbott Laboratories.

depression. The dose (3 to 6 cc.) of 5 per cent pentobarbital with curare (80 to 120 U) required for intubation was small and so the recovery period was short.

CHEMISTRY AND PHARMACOLOGY

Pentobarbital (nembutal) is ethyl (1-methylbutyl) barbituric acid and belongs to the group of short- (not ultra short) acting barbiturates. It is supplied by the manufacturer in 50 cc. bottles containing 50 mg. (¾ gr.) per cubic centimeter, is stable in solution, and multiple doses can be safely drawn from this stoppered bottle. Ampules are also available containing powder in 0.5 gm. (7½ gr.) dosage to be made up fresh with distilled water or saline. When administered intravenously its effects are seen almost instantly and may vary from drowsiness to complete anesthesia, depending on the total amount of the drug given and the individual reaction to it.

There is no *average* dose that can be relied upon to produce similar effects in different individuals. The barbiturates are among the worst offenders in regard to variability of dosage required to produce a certain depth of narcosis. The importance of this point is apparent. Pentobarbital *must* be given symptomatically, slowly (1 cc. per minute of 5 per cent solution was found satisfactory), remembering that the maximal depression is reached ten to fifteen minutes after the time of injection. Once in circulation it is beyond the reach of the anesthesiologist. If a conversation is maintained during this slow administration there is little danger of overdose and its accompanying respiratory depression. When the patient ceases to uphold his side of the conversation, he has bridged the gap between consciousness and unconsciousness—an additional 1 cc. is given and the needle withdrawn from the vein.

Usually the patient will sleep from thirty to sixty minutes, depending on the effect of the premedication and providing there is no painful stimulation. After ten to twenty minutes he can be aroused from this sleep by speaking in his ear slightly louder than normal. It should be remembered that the barbiturates are primarily hypnotics and do *not* possess analgesic properties except in anesthetic doses. Within the range of clinical use, the safety of pentobarbital intravenously is without question (if given slowly, 1 cc. per minute), for Abbott[4] reported injection of 1.5 to 2.5 gm. without mishap. He further stated that a dose of 30 to 40 per cent of this will produce hypnosis and 60 to 70 per cent of this dose (1.2 to 2.5 gm.) will produce complete analgesia.

We have found pentobarbital to be useful in conjunction with local or regional anesthetics. This is particularly true in patients under the influence of spinal anesthesia. In the nervous individual it allays the apprehensiveness so psychically traumatizing to the patient and so troublesome to the surgeon and anesthesiologist. Frequently patients become talkative under the influence of their preoperative sedation and annoy the surgeon to the point of distraction. A small, or sleep-producing dose of pentobarbital intravenously, just enough to produce unconsciousness, takes care of the situation perfectly.

Even though the patient is sound psychically and the local anesthesia is completely adequate for analgesia, this normal patient may become tired of the position or simply want to be blissfully asleep rather than aware of his surroundings and the clatter and chatter of the operating room. In such patients, the proper dosage affords a perfectly controllable method of providing this quietude and restfulness so gratifying to the patient. In fact, it is in the intravenous administration that the greatest advantage lies because only by this method is it possible to determine the dose accurately during the injection of the drug.

We believe one of its prime indications is in complementing spinal anesthesia as long as undue traction is not expected. It does not enhance laryngeal reflexes and one can safely insert an airway or pass a Levine tube without fear of laryngospasm. If it is necessary to inflict painful stimuli or heavy traction, these patients will thrash about on the operating table and offer considerable grief due to their incoherent state. If such a condition should occur, light nitrous oxide oxygen offers an easy and excellent supplement.

In combination with the other drugs used for preoperative sedation such as morphine and scopolamine, pentobarbital enhances the amnesic effect. Like other barbiturates, pentobarbital also affords a degree of protection against untoward toxic reactions occasionally seen as a part of conduction anesthesia.

COMMENT

Pentobarbital is conveniently drawn without mixing from the stoppered bottle making its intravenous use practical in the home, office, or anywhere else the physician may wish the immediate sedative or hypnotic effect of the short-acting barbiturate. Whether it is used to control convulsions or merely instantly to allay nervousness preceding a minor operation under local anesthesia, it should be remembered that each cubic centimeter of this stable solution contains ¾ gr. and therefore minimal doses should be given slowly (1 cc. per minute).

ADVANTAGES AND DISADVANTAGES

PENTOBARBITAL intravenously has a safe clinical range. A more accurate individualized dose is given by the intravenous route than by the oral or rectal route—and the effect is prompt and transient. It requires a minimum of apparatus and can be given in the patient's room with little fear of respiratory arrest or laryngospasm. Given preoperatively, it acts as a basal anesthetic and materially reduces the amount of other anesthetic agents required. In obstetric analgesia, when used with conduction anesthesia, the dose needed to allay restlessness does not appreciably retard the spontaneous respiration of the newborn infant. It is an excellent adjunct to spinal anesthesia without traction. It can be used for rapid hypnosis in the home, the amount being measured by using small doses. Repeated administration late in the operative procedure produces excessive postoperative restlessness.

If more sedation is needed than that provided by one intravenous dose of pentobarbital, barely sufficient to produce unconsciousness, then an *ultra* short-acting barbiturate such as pentothal repeated in small doses is preferable. It should be kept in mind when using intravenous pentobarbital in patients who are not to be hospitalized that the disorientation characteristic in those having had one of the barbiturates may appear briefly. It should *not* be used by a physician unwilling to take the time (1 cc. per minute) to give the drug slowly, for an overdose can easily be given with a rapid injection technic. It should not be used in patients with moist sounds (from any cause) in the lungs. High or low blood pressure is a contraindication to its use as is impaired renal function. Inability to find a vein is indirectly a contraindication which almost automatically bars children and obese adults.

SUMMARY

Pentobarbital (nembutal), a short-acting barbiturate supplied in powder or stable liquid form, is effectively used in conjunction with conduction anesthesia to produce amnesia or a light sleep safely. Its use as a sole anesthetic agent is to be condemned, for it is primarily a hypnotic and not an analgesic. Other uses are in obstetric analgesia, basal narcosis, premedication, induction prior to inhalation anesthesia, as an anticonvulsant, or in combination with curare for endotracheal intubation. When it is given slowly so that the dosage can be judged, it has a wide margin of safety. While it does not displace pentothal it does have some advantages over it for certain procedures as outlined.

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COMING MEETING

Association of Military Surgeons of the United States
1950 Convention, Statler Hotel, New York City, November 9-11. Program will deal with Civil Defense, Defense Role of the Physician, Aviation Medicine, Rehabilitation, Military Medicine, Surgery, Sanitation.

PRELIMINARY REPORT

RADIANT ENERGY AS A PROBABLE CAUSE OF Seasonal Changes in Specificity of Nonhemolytic Streptococci

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THE underlying reason for the occurrence often almost simultaneously over vast and isolated regions of epidemics due to or associated with alpha or nonhemolytic streptococci involving so predominantly the respiratory tract in winter and the central nervous system in summer in temperate climates is still obscure.

It is the purpose of this communication to summarize studies, which I have made, designed to contribute towards the solution of this problem. Studies in which primary isolations were made in mediums such as dextrose-brain broth which affords a gradient of oxygen tension and other favorable conditions for the growth of highly sensitive organisms resulted in the consistent isolation of respective specific type of nonhemolytic streptococci from persons having diverse nonepidemic[1] and epidemic[2-4] diseases. On appropriate inoculation of animals, the respective streptococci localized electively in the very tissues or organs corresponding to those effected in the patients from whom isolated. The different strains of streptococci on isolation in addition had distinctive cataphoretic velocity and specific serologic properties.

In epidemiologic studies, a truly remarkable seasonal parallelism in properties of nonhemolytic streptococci from various sources was found. The streptococci isolated from infection atria, exudates, and involved tissues of persons stricken, from indoor and outdoor air,[4] from milk[5] and water[6] supplies in winter months during epidemics of influenza and other respiratory infections had "pneumotropic" virulence. They localized electively in the respiratory tract on inoculation of animals producing pneumonitis in high incidence.[7] Streptococci isolated similarly from these diverse materials in summer during epidemics of encephalitis in human beings and encephalomyelitis in horses and other animals[3] and of epidemic poliomyelitis in human beings had "neurotropic" virulence. They localized electively in the brain or spinal cord of animals and produced lesions resembling spontaneously occurring encephalitis, encephalomyelitis, and poliomyelitis respectively.[2] The diplostreptococcus similarly isolated during epidemics of gastroenteritis had "enterotropic" virulence producing lesions electively in the mucous membrane of the stomach and intestines.[8]

The distribution curves of cataphoretic velocity of nonhemolytic streptococci isolated weekly for one year from the nasopharynges of two groups of well persons, from a composite milk supply cultured weekly and of four pure line strains of streptococci subcultured weekly changed seasonally and during sudden changes of weather in parallel manner in accord with streptococci isolated from nasopharynges of persons having respiratory infection in winter and from persons having encephalitis or poliomyelitis in summer.[9] Moreover, exposure of cultures of streptococci in test tubes sealed with cotton plugs to the high frequency field of radiant energy caused them to acquire cataphoretic velocity, animal virulence, and other properties similar to those of the streptococci isolated in studies of influenza, encephalitis, poliomyelitis, and arthritis, respectively, depending upon the degree of such exposure.[10]

These studies indicated that epidemics of influenza and other respiratory infections occur in winter and epidemics of encephalitis and poliomyelitis occur in summer in temperate climates because streptococci indigenous in well persons and in nature tend to acquire "pneumotropic" and "neurotropic" properties seasonally and that such changes may be due to radiant energy. A search was therefore made for a medium highly favorable for growth of streptococci which would remain neutral in reaction, in which streptococci would remain viable for many months permitting prolonged storage and in which a filtrable, perhaps

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the virus phase of the streptococcus, might develop. It was found that autoclaved chick-embryo medium fulfilled these requirements.[2, 11-13]

On prolonged storage of streptococcal cultures in this medium layered with oil and sealed with cotton plugs, screw caps, or rubber stopples, changes in localizing and serologic properties occurred seasonally in accord with streptococci associated with or the cause of epidemics of influenza, encephalitis, and poliomyelitis.[2, 11, 12] In order to determine whether such seasonal changes are due to radiant energy as would seem, cultures of different types of streptococci and pneumococci in autoclaved chick-embryo medium, sealed in glass ampules, were stored seasonally, geographically in thin walled metal casings within fiber cartons at ground level where shortwave radiant energy is constantly present in varying degree and in a silver mine at Kellogg, Idaho, 5,000 feet under limestone where radiant energy was not demonstrable. In addition, the respective strains of streptococci and pneumococci were stored at ground level in Rochester, Minnesota, dried on glass balls, kept frozen in dry ice and at 10° C. dehydrated in dense suspensions of glycerin, 2 parts, and saturated sodium chloride solution, 1 part, in which it was found, in previous studies, that antigenic specificity was preserved for years and viability for months.

Three such long-lasting storage experiments were performed. In the first experiment, 4 strains of nonhemolytic streptococci, 2 of "neurotropic" type isolated from the spinal cord of monkeys that succumbed to experimental poliomyelitis following inoculation of virus and 2 of "pneumotropic" type isolated from the blood of a case of acute influenza and from freshly fallen snow during an epidemic of influenza were stored at ground level for nine months from May to February into respective epidemics of respiratory infection in Rochester, Minnesota, overlaying and in the mine. The 2 neurotropic strains had changed to pneumotropic type and the 2 pneumotropic strains remained pneumotropic on storage at ground levels into respective epidemics of respiratory infections. No change in type occurred on storage in the mine and it took six weeks of storage at room temperature at ground level in Rochester, Minnesota, for the neurotropic strains that remained neurotropic in the mine to change to pneumotropic type during an epidemic of respiratory infection.[9] The pneumotropic strains again remained pneumotropic. Hence, shipment of cartons, containing the cultures to and from Rochester for study, by regular or air mail was permissible.

In the second experiment, 22 sets (each consisting of 14 strains) of chick-embryo cultures sealed in glass ampules were similarly stored geographically at ground level chiefly in bacteriologic laboratories of health departments or in hospital wards in different parts of the United States, Alaska, and Hawaii and as a control in the mine.*

Seven of the strains were nonhemolytic streptococci, 4 of pneumotropic, and 3 of neurotropic type. Two were of Type I and one each of Types II and III pneumococci and 3 were hemolytic streptococci, group 4. Cultures were made in Rochester, Minnesota, after spring-into-summer storage and after additional storage from summer into winter. Of the large number of subcultures made and studied after spring-into-summer storage, 82 per cent of nonhemolytic streptococci of pneumotropic type, 56 per cent of hemolytic streptococci, and 28 per cent of pneumococci changed to nonhemolytic neurotropic type, and the neurotropic nonhemolytic streptococci remained neurotropic.

In sharp contrast, after further storage from autumn into winter, all cultures originally pneumotropic remained pneumotropic. Seventy-two per cent of cultures of nonhemolytic streptococci originally neurotropic and all pneumotropic strains that had acquired neurotropic properties on summer storage, 42 per cent of hemolytic streptococci and 58 per cent of pneumococci, had changed to pneumotropic type. No change in type occurred in control cultures stored in the mine and no significant changes occurred in one set of cultures stored at ground level in Rochester in a safe in which radium was kept. The walls of the safe, 5 inches thick consisting of one inch of lead and about 4 inches of fire clay and of sheet steel, sufficed to shield the cultures from the effective radiant energy.

In the third experiment, 3 sets of chick-embryo cultures sealed in glass were prepared in February from the same 14 strains studied in the second experiment that meanwhile had been kept frozen in dry ice. Two sets were stored in Rochester, one at room temperature, the other at 34° C. through February into an epidemic of respiratory infection and one in the mine. The 4 strains of nonhemolytic streptococci of pneumotropic type remained pneumotropic and the 3 neurotropic strains changed to pneumotropic type on storage at ground level and no change occurred in the control cultures stored in the mine.[9]

The data obtained in these studies indicate that some influence other than barometric pressure, humidity, and temperature is operative at ground level in temperate climates in causing alpha or nonhemolytic streptococci and to a lesser degree hemolytic streptococci and pneumococci in chick-

*Grateful acknowledgment is hereby made for the cooperation of health officers, physicians, hospital superintendents, the Sunshine Mining Co., Kellogg, Idaho, Dr. Alexander Goetz of The California Institute of Technology, and Dr. M. M. D. Williams of the Department of Biophysics of the Mayo Foundation.

embryo medium cultures to change seasonally and to acquire neurotropic properties in summer characteristic of streptococci associated with epidemic encephalitis, encephalomyelitis, and poliomyelitis and of influenza and milder types of respiratory infections in winter months. This influence was not operative in the mine where short wavelength radiation was not demonstrable nor in a safe at ground level. Moreover, the streptococci kept frozen in dry ice, dried on glass balls, partially dehydrated in glycerin, 2 parts, and saturated sodium chloride solution, 1 part, at 10° C. also did not change. A low-grade metabolism appears essential for such changes to occur.

It is postulated that the seasonal changes which occurred at ground level in these organisms and therefore presumably in persons and in nature during respective epidemics were due to a physical agent, radiant energy, which probably comes from the sun, capable of passing through thin sheets of glass and metal but not through one inch of lead and hence not due to the highly penetrating cosmic radiation. The varying length of time necessary to complete the pneumotropic to neurotropic and reverse cycle might be due to (1) a seasonal variation of the intensity of the physical agent which does not occur in tropical regions where such epidemics do not or occur far less often; (2) variations in inherent properties and the rate of reproduction of the organisms, or (3) what is most likely a combination of these.

If such influence be really operative in nature the seasonal incidence of epidemics, especially epidemics such as influenza and poliomyelitis that often occur almost simultaneously over vast and isolated regions, becomes more explicable in that such epidemics arise owing to seasonal changes in temperate climates in streptococci indigenous in the subjects and in nature and that aerial and contact infection may play a minor role. Active and passive immunization with respective harmless specific vaccines, antigens, antiserums, or thermal antibody[14,15] in advance of or abreast with anticipated seasonal recurrent epidemics may prove necessary in addition to the usual measures now directed for their control.

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COMING POSTGRADUATE COURSES

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CLINICAL STUDY

An Improved Vaginal Cream in the Practice of Gynecology

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Successful treatment of the various leukorrheas requires a careful survey of the history and a knowledge of gross alterations in the genital tract. Bacterial agents play a major role as etiologic factors and each produces changes in the vagina characteristic of such etiology.

A review of the medical literature reveals the need for a safe and effective therapeutic agent to treat vaginitis and cervicitis, as well as to prepare the vagina for minor and major surgical procedures.

It is apparent that a substantial part of gynecologic practice deals with the treatment of vaginitis and cervicitis. There is evidence that chronic cervicitis is being treated by some form of cautery or conization as an office procedure. Before such a procedure is resorted to, the physician should make an effort to reduce and control the infection by medical treatment.

The ideal treatment for the condition indicated should provide (1) quick symptomatic relief; (2) a safe and easy method that can be carried out mostly by the patient to reduce office visits to a minimum, and (3) a wide margin of therapeutic effect to cover a broad range of infections.

Parks[1] recommended allantoin-sulfanilamide-lactose in a special greaseless base as a convenient and effective method of treating many ulcerative lesions of the lower genital tract. Using the same cream, Smith[2] found it effective in nonspecific infections of the vaginal tract. Horoschak and Horoschak[3] found this combination to be the most effective treatment of endocervicitis they had found. In spite of these enthusiastic reports, the preparation did not completely fulfill the provisions listed. It was found that monilial vaginitis did not respond to treatment with the above combination.

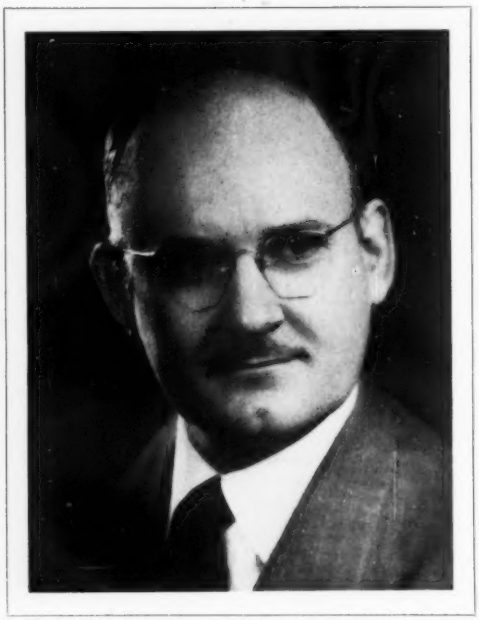
About eighteen months ago it was suggested that the vaginal cream be improved by the incorporation of 9-aminoacridine, 0.2 per cent, the rest of the formula remaining the same.

Unger and Robinson[4] found 9-aminoacridine to be active against Gram-positive cocci and spore-bearing anaerobes, as well as against Gram-positive and Gram-negative bacilli. Goetchius and Lawrence[5] reported on the marked bactericidal effect of 9-aminoacridine against anaerobic organisms.

McIntosh and Selbie[6] recommended, following their extensive work, ointments and mixtures of sulfonamides and the acridine antiseptic in a ratio of 100 parts of the first to 1 part of the second.

It was decided to try to formulate a treatment to meet the provisions set forth by using allantoin 2 per cent, sulfanilamide 15 per cent, and 9-aminoacridine 0.2 per cent, in a water-miscible base with an acid reaction.*

*Allantomide Vaginal Cream (Improved), supplied by the Medical Research Department, The National Drug Company, Philadelphia.



HUBERT A. HENSEL

PATIENTS STUDIED AND PLAN OF TREATMENT

There were 143 patients from private practice classified as follows:

Trichomonas vaginalis vaginitis	39
Monilial infections	32
Nonspecific vaginitis (due to mixed organisms)	12
Chronic cervicitis with conization	25
Before and after vaginal surgery	20
Before and after abdominal complete hysterectomy	15

TREATMENT OF VAGINITIS

Only cases that presented symptoms with positive physical and laboratory findings are included in this study.

Most of the cases of vaginitis, whether trichomonal, monilial, or nonspecific, were treated essentially in the same manner. Early in the study, severe cases of moniliasis were painted with 5 per cent gentian violet in 20 per cent alcohol on the first visit, but this was discontinued and results seemed as good.

Vaginal smears and droplet examinations were made in every case. If tissues were not too irritated, bimanual examination was carried out. The patient was given a description of her trouble and instructed to douche morning and night with 2 ounces of vinegar per quart of hot water. After the douche, an applicator of the allantoin-sulfanilamide-9-aminoacridine cream was introduced into the vagina. This treatment was continued through the menstrual period. The patient was told she could dispense with the douche during her menstrual period, but more effective results would ensue if the douche was continued.

After two weeks, if symptoms were alleviated, the treatment was continued once daily for two weeks. Douches were advised about 3 times weekly. Fifty tablets of mandelamine were taken at the rate of 2 with each meal and at bedtime to eradicate any possible Trichomonas or Monilia in the bladder or urethra.

Every effort was made to impress the patient with the importance of continuous treatment and to continue treatment even after cessation of symptoms to prevent recurrences.

A prerequisite to treatment was the questioning of the patient as to any previous use of sulfonamide drugs and any possible sensitivity to them. The cream was not used in 2 cases that gave histories of reaction to former administration of sulfonamides.

TREATMENT OF CHRONIC CERVICITIS

The patients with chronic cervicitis were treated in essentially the same way except that mandelamine was not given unless there was a vaginitis. About two weeks after the start of the above treatment, or between the end of the period and before ovulatory time, the cervix was coned with a cold cautery unit. Instead of coagulating the bleeding points, a piece of absorbable hemopack was introduced into the canal. This usually controlled bleeding and reduced incidence of hemorrhage when the coagulating area would slough. Twenty-four hours after conization, the vaginal douche and instillation of allantoin-sulfanilamide-9-aminoacridine vaginal cream were started and continued for two weeks.

All cases healed quickly and cleanly, and the usual backache and pain in the side accompanying this procedure were eliminated.

VAGINAL SURGERY AND HYSTERECTOMY

In cases where vaginal surgery or abdominal complete hysterectomy was planned, the same procedure—vinegar douche and application of

allantoin-sulfanilamide-9-aminoacridine cream as outlined before—was used for two weeks prior to surgery. If senile vaginitis was present, estrogens and vitamin A were also used. The morning of surgery, a douche of potassium permanganate (1:300) was used to cleanse the vagina of all of the cream. Starting on the third postoperative day, a saline douche was given daily followed by topical application of the vaginal cream.

RESULTS AND COMMENTS

Trichomonas vaginalis vaginitis (39 patients)—All of the patients were quickly relieved of vaginal irritation. Three patients required a second course of treatment several months after cessation of the first. All of the remaining patients were negative to bacteriologic examination two months after stopping treatment. Some of these cases were also treated with conization for chronic cervicitis to remove possible foci of infection.

Vaginal moniliasis (32 patients)—The patients in this group responded more slowly than those with trichomoniasis, probably because most of them showed more local reaction to the infection. In many of the patients the vaginal epithelium was hypertrophic, and gave the appearance of multiple small verruccae over the vaginal surface. Some of these patients had been under treatment elsewhere for vaginal warts, and one patient had been advised that excision with cautery was necessary.

After one week of treatment, even the patients with the most severe symptoms showed remarkable improvement; after two weeks, the vaginal mucosa appeared quite normal. Symptomatic improvement was experienced by the patients with mild monilial infections within several days. There was a recurrence in 2 of the patients shortly after discontinuing therapy. One patient continued using the cream for six months without manifesting any toxic reactions. One case had a positive sugar.

Nonspecific vaginitis (12 patients)—Gram-negative organisms predominated as etiologic factors in a majority of these patients. All responded quickly to treatment and were symptom-free in approximately one week. Two patients were referred cases who had been vigorously treated with many different medications. Probably most of the severe irritation in these patients was due to previous overtreatment. These patients obtained symptomatic relief quickly and felt well in several days. One of the patients had folliculitis of the vulva which responded more slowly to the therapeutic procedure followed.

Conization of the cervix (25 patients)—All of these patients had severe chronic cervicitis. Reasons for using the allantoin-sulfanilamide-9-aminoacridine vaginal cream in these patients were to: (1) reduce the incidence of infection; (2) prevent acute flareups after conization; (3) stimulate healing, and (4) reduce sloughing.

Results in these cases were excellent. Twenty of the patients were treated in the office and 5 were hospitalized. One of the 5 required suture repair of bilateral laceration; 4 required too radical conization to be done without anesthesia. Two patients had to be seen eight to ten days after cautery for troublesome bleeding. Not one patient complained of aggravation of her original symptoms.

Most of the patients were healed in two weeks and all in four weeks. In no case was there a resulting stenosis. One patient developed a granulating area at the external os which required cauterization. The usual sloughing discharge was greatly reduced in this group.

Vaginal surgery (20 patients)—This group includes vaginal hysterectomies and anterior and posterior repairs.

The reasons for using the allantoin-sulfanilamide-9-aminoacridine vaginal cream in these patients were to: (1) reduce postoperative morbidity; (2) hasten healing, and (3) decrease amount and odor of vaginal discharge postoperatively.

In this group of patients, which included 12 vaginal hysterectomies and 8 anterior posterior colporrhaphies, the morbidity was definitely lowered. The ages of the patients ranged from 30 to 70 years. Early rising was used on this group and all were up slowly, starting on the second and third days. Seven patients did not have an elevation of temperature over 100° F. at any time during the postoperative hospital stay.

The temperature peak in most cases occurred on the first and second days postoperatively and started to approach normal about the third day. Ten cases (50 per cent) spiked to temperatures between 100.2° F. and 101.8° F. on the first and second days, started to drop on the third day

and were under 100° F. thereafter. This would be expected as a reaction to surgery and not as a result of the infection. One patient's temperature rose to 102° F. on the second day with a fall to normal on the third day and until the seventh day when she developed a bilateral pyelitis with a temperature of 103° F. This patient, who had vaginal hysterectomy, had a rough course and discharged from the vaginal vault for three months but finally healed. Two cases spiked a temperature daily throughout twelve days to 101.4° F. and 102.8° F., but otherwise had uncomplicated courses. Operative results have been good in all these cases up to the present time. The healing was improved in comparison to patients with the same care but without the use of the vaginal cream. The vaginal discharge was greatly reduced and the unpleasant odor was eliminated.

One patient developed generalized pruritus after several instillations of the vaginal cream. Her history revealed a sensitivity to sulfonamides. The reaction cleared up within thirty-six hours after curtailing treatment with the vaginal cream.

Abdominal hysterectomies, complete (15 patients)—The reasons for using the allantoin-sulfanilamide-9-aminoacridine vaginal cream in this group were: (1) to reduce to a minimum the bacterial count in the vagina, thus increasing the safety of abdominal total hysterectomy, and (2) to prevent infection of the vaginal cuff and the pedicles, postoperatively.

Although the number of patients in this group is too small to be statistically significant, the technic used was worth while. None of the patients developed postoperative complications. The vaginal vault healed well and one month postoperatively, the cuff closed over in all of the patients.

base buffered to an acid reaction, was used in the treatment of Trichomonas vaginalis vaginitis, monilial vaginitis, nonspecific vaginitis, chronic cervicitis treated with conization, vaginal surgery (pre- and postoperatively), and abdominal hysterectomies (pre- and postoperatively).

The favorable response of every patient reflects both the efficacy of the cream and the fact that this group of patients was apparently unusually cooperative in following the prescribed course of treatment.

Symptomatic and bacteriologic cures were obtained in all of the 39 patients with Trichomonas vaginalis vaginitis. Three of these patients required a second course of treatment to obtain the desired clinical result.

In monilial vaginitis, the vaginal cream was found to be more effective than any other agent the author had used previously. Every one of our 32 patients with moniliasis was relieved of this usually stubborn condition.

All 12 patients with nonspecific vaginitis obtained symptomatic relief within two days and were symptom-free in approximately one week.

Preparatory treatment with the allantoin-sulfanilamide-9-aminoacridine vaginal cream resulted in a smooth postoperative course in conization of the cervix and in vaginal surgery. Sloughing was reduced and the odor and discharges were readily controlled.

The allantoin-sulfanilamide-9-aminoacridine vaginal cream provides an easy, safe, and pleasant treatment which can be carried out by the patient.

Its use for six months in 1 patient caused no toxicity.

Only 1 patient in 143 showed a sensitivity reaction which was mild and cleared up when the cream was discontinued.

Note: Two reports have appeared since the preparation of this report has been completed:

Dill, L. V., and Martin, Shirley S.: The use of a vaginal cream containing 9-aminoacridine in the treatment of mycotic vaginitis. M. Ann. District of Columbia.

Cacciarelli, R. A.: Acridine-sulfonamide therapy of trichomonas vaginitis. J. M. Soc. New Jersey 46:87 (February) 1949.

SUMMARY

An improved vaginal cream containing allantoin 2 per cent, sulfanilamide 15 per cent, and 9-aminoacridine 0.2 per cent, in a water-miscible

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Pediatrics

IN GENERAL PRACTICE

For general practitioners, in whose practice is included a major proportion of the medical management of infants and children, and for the specializing pediatrician as well, POSTGRADUATE MEDICINE *presents this special regular department devoted to brief discussions by recognized authorities on their preferred methods of the treatment and management of diseases and problems of infancy and childhood.*

The Management of Heart Disease in Children

STANLEY GIBSON

CHILDRENS MEMORIAL HOSPITAL, CHICAGO

GIBSON

THE great majority of instances of heart disease in children are due either to congenital malformations of the heart or to rheumatic fever.

The recent brilliant advances in the surgery of congenital cardiovascular anomalies have brought new hope to victims of several types of malformations. In the group which is unaccompanied by cyanosis, patent ductus arteriosus, coarctation of the aorta, and vascular ring due to double aortic arch have been relieved by surgical means. In the cyanotic group, the tetralogy of Fallot, tricuspid atresia, and congenital pulmonary stenosis with intact ventricular septum have been much improved by surgical intervention.

There are, however, many types of congenital cardiac defects which at present are not amenable to surgery. Some of these are so mild as to cause little or no handicap, whereas others are so severe that the child is seriously incapacitated. Inasmuch as the physician feels that the basic pathology cannot be altered, he sometimes fails to give these patients the attention to which they are entitled. Much can be done to increase the patient's comfort, and often to prolong his life. He should be protected from exposure to respiratory or other infections. He should have the usual inoculations which are recommended for normal infants. Because of the poor circulation, extremes of heat and cold are not well tolerated.

Infections should be promptly and vigorously treated because of the ever present danger of bacterial endocarditis. Sulfonamide drugs or penicillin should be given for 24 hours before such surgical procedures as tonsillectomy or extraction of teeth, and for two or three days thereafter. Tooth extraction is a particularly dangerous procedure unless these precautions are taken. Although the majority of cases of bacterial endocarditis may respond to antibiotic therapy, the treatment is long drawn out and recovery is by no means certain.

Heart failure is not infrequent in the more severe cases and should be treated by digitalis in doses appropriate to the child's weight. One cat unit for each 10 pounds of body weight is the amount usually considered adequate for digitalization. One-half the amount is given as the initial dose, and the remainder given in divided doses at six-hour intervals. The daily maintenance dose is about one-tenth of that which is required for

digitalization. It should be emphasized, however, that children vary widely in their tolerance for digitalis. Hence the patient should be watched for signs of digitalis intoxication, but the drug should be pushed to the point where a therapeutic effect is obtained or where signs of intoxication compel its omission.

Paroxysmal dyspnea is a particularly distressing occurrence in the more severe forms of congenital heart disease. It consists of attacks in which the patient becomes restless, extremely cyanotic, limp, or even unconscious. These attacks, while usually of short duration, are terrifying to the parents, and may terminate fatally if unrelieved. The treatment consists in placing the patient face down with the knees drawn up under him, administration of oxygen, and hypodermic injection of morphine in dosage appropriate for his weight. These measures usually afford prompt relief.

In the over-all management of congenital heart disease, the mistake most frequently made is that of attempting to restrict the child's activities unnecessarily. It must be remembered that the child has had his handicap from birth, and as he becomes active, he discovers his limitations. He will, therefore, stop of his own accord when he becomes fatigued or short of breath. To attempt to restrict him beyond this point meets with scant success, makes him acutely unhappy, and is furthermore unwise. It goes without saying that group activities or competitive games should be omitted if they are found too tiring.

The management of rheumatic heart disease presents an entirely different picture from that of congenital heart disease, inasmuch as we are not dealing with a static condition, but one in which the picture may be constantly changing.

At the onset of rheumatic fever, even without evidence of heart disease, the patient should be put to bed and kept there until signs of rheumatic activity have subsided. If signs of cardiac involvement occur, the period of rest will necessarily be prolonged. At the onset, salicylates should be administered until the patient is comfortable and free of fever. Whether salicylate therapy should be continued for a longer time, in the hope of lessening the amount of cardiac damage, is still a disputed question. At least it should be remembered that salicylates may mask the symptoms of rheumatic fever, so the drug should be withdrawn and the patient observed for a period before it can be assumed that convalescence has begun.

ACTH AND CORTISONE

The recent introduction of ACTH and cortisone has brought high hope that these drugs may be effective in the treatment of rheumatic fever. Reports to date indicate that they produce a prompt alleviation of symptoms in the recent acute cases. Joint pains disappear, the fever subsides, the patient feels better, heart murmurs may diminish or disappear, and electrocardiographic abnormalities may return to normal. That it is not curative is evidenced by the fact that symptoms and signs may recur when the drug is discontinued. There is some evidence, however, that ACTH or cortisone tends to inhibit the proliferative changes which are chiefly responsible for scarring of the heart muscle and valves.

In severe chronic rheumatic heart disease where congestive heart failure is threatened or present, these drugs have proved valuable in tiding the patient over a critical period. It therefore seems that ACTH and cortisone may be of value in aborting in some degree the early acute manifestations of rheumatic fever and also be life-saving in severe chronic rheumatic heart disease. This therapy is still in its infancy. Many more patients will have to be studied, together with a long term follow-up, before the final answer can be given.

RECURRENT RHEUMATIC INFECTION

Once the active infection has subsided, and the child has again become active, the question of recurrent rheumatic infection confronts us. Numerous reports have shown pretty conclusively that sulfadiazine, or a similar preparation, administered in the dosage of ¼ to ½ gm. twice daily has been effective in preventing recurrences in a very high percentage of cases. If this regimen is undertaken, it should be carried out faithfully and without intermission for a period of years, the duration depending to some extent on the age of the patient and the amount of time which has elapsed since the last rheumatic episode. Because of the possibility of untoward side effects, the patient must be seen at frequent intervals, and examination of the blood and urine carried out.

It is possible that in the near future oral penicillin will replace sulfonamide drugs for prophylaxis. It has already been shown that the administration of penicillin in the first few hours of an acute hemolytic streptococcic infection of the throat is effective in preventing a recurrence of rheumatic fever in a high percentage of patients. Sulfonamides have not been found to be effective in this situation.

In emphasizing these special measures, one should not lose sight of the general care of the patient. Adequate diet, sufficient clothing, satisfactory living conditions, and general hygiene each have an important place.

PAROXYSMAL TACHYCARDIA IN INFANCY

In conclusion I wish to mention one functional

disturbance of the heart which constitutes a real pediatric emergency. I refer to paroxysmal tachycardia in infancy. It is most frequent during the first month of life. The heart rate is usually between 250 and 300 per minute. If untreated, cardiac failure with a fatal termination is not infrequent. Digitalis is the drug of choice. Rapid and full digitalization should be carried out and continued until the heart returns to normal rhythm. Paroxysmal tachycardia in older children is a less serious condition, and in most instances is controlled more readily with quinidine than digitalis.

Treatment of Tuberculosis in Children

LEE FORREST HILL

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HILL

Diagnosis of a tuberculous lesion in a child raises the question at once as to whether or not some form of specific therapy should be instituted in addition to the familiar methods commonly employed before the present chemotherapeutic and antibiotic era. In general it may be said that all forms of tuberculosis, except those which have a good prognosis without specific therapy, should be so treated. This will include miliary and meningeal tuberculosis, tuberculous bronchopneumonia, severe progressive primary tuberculosis, chronic pulmonary reinfection tuberculosis and such extrapulmonary forms as renal, bone and joint, adenitis with or without draining sinuses, tuberculous laryngitis, peritonitis and tuberculous ulceration of the intestine. Mild forms of primary tuberculosis with or without calcification in the lungs and tracheobronchial lymph nodes should not be treated chemotherapeutically, at least with streptomycin, nor should chronic pulmonary reinfection tuberculosis which has a good prognosis with or without collapse therapy.

In the last decade extensive in vitro and in vivo studies have been carried out with such drugs as DIASONE, PROMIN, PROMIZOLE, para-aminosalicylic acid, streptomycin, dihydrostreptomycin, neomycin, and more recently in Europe with the thiosemicarbozones, of which CONTEBEN seems to be the most effective. Up to the present time streptomycin or dihydrostreptomycin, either alone or in combination with promizole or para-aminosalicylic acid or both, are the drugs in most common clinical usage against all types of tuberculosis in children where specific therapy is indicated.

Streptomycin has several disadvantages. It is neurotoxic especially to the eighth nerve and to its vestibular branch Large doses continued over a period of several weeks are very likely to result in permanent deafness. Smaller doses, such as are now in current use, are seldom followed by deafness. However, damage to the vestibular apparatus with ataxia almost invariably occurs, but disappears after cessation of the drug in many of the cases. Fortunately loss of the sense of equilibrium from vestibular damage is not a serious handicap and children adjust to it.

A second disadvantage of streptomycin is its tendency to permit the development of resistant strains of tubercle bacilli. When this occurs, the patient suffers a relapse and streptomycin is no longer effective. The time of emergence of resistant strains varies. Experience has shown that this will have occurred in 50 per cent of the cases by the end of 60 days of treatment. Dihydrostreptomycin offers no improvement so far as drug-resistance is concerned, but neurotoxic damage may be lessened or delayed in the time of its appearance.

Combining such drugs as promizole or para-aminosalicylic acid or both with streptomycin considerably reduces the frequency of emergence of resistant strains. Each of these drugs is bacteriostatic against the tubercle bacillus and in combination with streptomycin the claim is made by some that the effectiveness of each is enhanced. Streptomycin is a relatively quick-acting drug while promizole is slower, but the effect of promizole in keeping down resistant strains permits the longer use of streptomycin. This latter fact is of chief

importance in treating the more severe forms of tuberculosis in children such as meningitis where prolonged therapy is imperative.

TUBERCULOUS MENINGITIS

Lincoln[1] has attained remarkable success in the treatment of this form of tuberculosis which prior to streptomycin was uniformly fatal. Up to July, 1949, out of a total of 18 children who had completed streptomycin therapy but were still on promizole, 13 survived 9 to 27 months after the initial diagnosis. The other 5 had died, giving a survival rate of 72 per cent. The therapeutic regimen used by Lincoln consists of 1.0 gm. daily of streptomycin intramuscularly for 180 days regardless of age and weight. For the smaller and more frail children, 0.5 gm. is given every 12 hours, but for older, well-nourished children, it is given once a day. In addition, 0.1 gm. of streptomycin is given intrathecally daily for 40 injections unless mechanical difficulties develop or toxic symptoms occur in which case the dose is reduced to 0.05 gm. to 0.1 gm. given every second or third day. But intrathecal treatment is continued until the 40 injections are completed. Promizole is combined with intramuscular and intrathecal streptomycin and is continued for a period of three years. The recommended dose of promizole is that amount which will produce a blood level of 1.0 to 3.0 mg. per 100 cc. Initially 0.5 to 1.0 gm. daily is given by mouth at six-hour intervals. If no toxic symptoms are encountered the dose is raised until the desired blood level is reached. Lincoln found that this varied from 0.375 gm. to 8.0 gm. daily.

In support of the use of streptomycin intrathecally, Lincoln cites the report of the British Medical Research Council[2] to the effect that combined intramuscular and intrathecal therapy cured more cases than did intramuscular treatment alone. For the use of promizole for three years, she advances several reasons. One of the most important is that it reduces the risk of relapses which so commonly occur when streptomycin is used alone. Promizole was found to be ineffective when used as the sole agent in treating tuberculous meningitis, but 5 cases out of 7 of acute generalized miliary tuberculosis in children resulted in complete remission in 6 to 12 months. These 5 children are well three to five years after treatment was begun. Thus promizole was demonstrated to have tuberculo-bacteriostatic activity in its own right, but was unable to cope with meningitis. Lincoln is also of the opinion that toxic reactions are less marked from promizole when it is used in combination with streptomycin than when it is used alone. Vomiting and cyanosis are the early toxic symptoms. Leukopenia occasionally occurs as does enlargement of the thyroid gland with elevated cholesterol. Breast and nipple enlargement occurred in one patient. A cherry-red or pink urine of unknown etiology was seen in most patients receiving promizole.

In Lincoln's series, 4 patients became deaf while on streptomycin therapy, but 2 recovered their hearing. Since the meningitis itself may produce deafness, it is impossible to fix the blame with certainty in any case of tuberculous meningitis being treated with streptomycin. All patients developed vestibular disturbance as shown by the caloric (Kobrak) test, but 4 out of 5 of the children had regained a normal response by one year after cessation of streptomycin. Urticaria occurred in 4 patients, developing into exfoliative dermatitis in one.

Toxic effects of intrathecal streptomycin are sometimes severe. Lincoln lists the severe reactions as convulsions, opisthotonos, general muscular rigidity, or sudden high fever and marked drowsiness followed by prolonged sleep. Less severe reactions include vertigo and ataxia, transient strabismus or nystagmus and projectile vomiting. Levinson[3] maintains that intrathecal injections of streptomycin are unnecessary. He reports a series of 19 cases of tuberculous meningitis treated with 1.6 gm. of streptomycin daily injected intramuscularly for 90 days. Examination of the spinal fluid showed effective levels of streptomycin in a majority of the patients. Eleven of the children died and 8 were living at the time the article was written.

Jones and Howard[4] have also had excellent results in the specific treatment of children with various forms of tuberculosis. Out of 101 streptomycin-treated cases over a two-year period, only one death has occurred as compared to a mortality rate of 9.8 per cent among 780 cases observed in the pre-streptomycin period from 1941 through 1946. Among the 101 cases were 12 of miliary tuberculosis, 4 of combined miliary tuberculosis and meningitis, and 5 of meningitis. The one fatality was in the miliary-meningitis group.

Streptomycin alone was used by Jones and Howard according to the following regimen: For tuberculous meningitis the intramuscular dosage was 55 to 88 mg. per kilogram of body weight per day for four to six months depending upon the clinical and spinal fluid response, and then 22 to 44 mg. per kilogram of body weight per day for the remainder of the six-month period. The daily dose was divided into 2 or 3 injections. Intrathecally 2.5 mg. per kilogram, with a limit of 50 mg., was given daily for three weeks, then the same dose three times per week for three months. The dose was then cut in half and given twice a week for two months. If complications prevented the giving of intrathecal injections, the intramuscular dose was increased to 100 mg. per kilogram per day. Neither promizole nor para-aminosalicylic acid was combined with the streptomycin. Five children with tuberculous

meningitis have been sent home as recovered cases 26 to 19½ months after the onset of the meningitis.

MILIARY TUBERCULOSIS

Miliary tuberculosis has a better prognosis from specific therapy than does tuberculous meningitis. A combination of the two gives the worst prognosis. Since tuberculous meningitis not infrequently develops during the course of miliary disease this contingency must constantly be watched for in order that specific therapy for the meningitis may be started as early as possible. In the treatment of miliary tuberculosis Lincoln[5] uses 1.0 gm. of streptomycin intramuscularly for 120 days and combines with it promizole in the same dosage as for tuberculous meningitis. Jones and Howard[4] treated 12 cases of miliary tuberculosis without a fatality using the same dosage schedule of streptomycin as for tuberculous meningitis, except, of course, with the omission of the intrathecal injections.

Relapses during or following the initial course of streptomycin therapy in either tuberculous meningitis or miliary tuberculosis necessitate a second or even a third course of streptomycin.

OTHER FORMS OF TUBERCULOSIS

All observers agree that streptomycin is contraindicated in the types of childhood tuberculosis which have a good prognosis without specific therapy. Thus primary tuberculosis either in the early pneumonic stage or in the later calcified stage should not be treated with streptomycin because of the risk of the development of resistant organisms which would not be amenable to treatment in the event of a later extension to a more serious form of the disease or of the transmission of resistant organisms to other persons. However, a severe pulmonary extension of a primary lesion or a bronchogenic spread with tuberculous bronchopneumonia should be treated with streptomycin. Extrapulmonary and extrameningeal forms of tuberculosis such as renal, laryngeal, bone and joint, intestinal, tuberculous cervical adenitis with or without draining sinuses, and other tuberculous sinuses should be treated with streptomycin. The dosage required is smaller and the course of treatment shorter.

For cases other than meningeal and miliary, Lincoln[5] uses streptomycin on a weight basis. Thus, for children under 10 pounds in weight the daily dose is 0.3 gm.; 10 to 19 pounds, 0.4 gm.; 20 to 39 pounds, 0.5 gm.; 40 to 59 pounds, 0.6 gm.; 60 to 89 pounds, 0.75 gm.; and 90 pounds and over, 1.0 gm. If treatment has to be continued longer than a few days, promizole is added. Most cases selected for treatment were those in which improvement could be expected within six weeks. An occasional case was treated for 90 or even 120 days.

Included among the extrapulmonary and meningeal group treated by Jones and Howard were 13 bone and joint cases, 2 with adenitis and draining sinuses, 2 with pleuritis, 2 with peritonitis, 1 with pericarditis, and 1 with renal tuberculosis. The dosage schedule of streptomycin for these types of cases was 15 to 33 mg. per kilogram daily for four to seven days, and then three days per week for a total of 42 or 84 dose-days, depending on the response. Lincoln, Jones and Howard, as well as other authors, stress the point that streptomycin does not replace the other indicated therapeutic measures.

Immobilization is carried out for tuberculosis of bones and joints as always and abscesses are drained surgically. Cervical glands may need to be excised, but with streptomycin it may be expected that draining, disfiguring sinuses will be healed or prevented.

In chronic pulmonary reinfection tuberculosis in children, streptomycin should not be used if the lesion or lesions are minimal, and the outlook is good with or without collapse therapy, but in more extensive involvement in the exudative stage a course of streptomycin may make it possible for collapse or other surgical procedures to be used.

Undoubtedly, as further experience is gained, modifications in the treatment schedules as outlined will be made. Very likely, new drugs superior to those now available will be discovered, perhaps in the near future. But until such a desirable goal is forthcoming it would seem advisable for the average practicing physician to employ those methods which at present appear to be yielding the best results. Our own cases of tuberculosis in children are too few in number to permit drawing conclusions, but those we have had, have been treated according to the recommendations of Lincoln. A 15-year-old boy with tuberculous meningitis made an initial satisfactory recovery, but died some six months later in a relapse which failed to respond to a second course of streptomycin. Several other younger children, also with tuberculous meningitis, are progressing satisfactorily under treatment at the present time. To those of us who in the past have had repeatedly to stand hopelessly and helplessly by in the face of fatal forms of tuberculosis, it is a gratifying experience indeed to have at least some promising tools with which to work.

But lest we become too optimistic, let us remember that it is too early to predict the final score with such a formidable antagonist as tuberculous meningitis. Many more months or even years of follow-up will be necessary before it will be possible to say that recoveries are real and permanent, and not apparent. And of those that do survive not all will be normal children. Mental deficiency, deafness, blindness and various types of paralysis will be the fate of an unfortunate few.

SUMMARY

It may be said that streptomycin is the drug of choice for the treatment of all forms of tuberculosis in children for whom specific therapy is indicated. Because of the excellence of her results, the dosage schedules as employed by Lincoln are recommended. For tuberculous meningitis, miliary and hematogenous tuberculosis, streptomycin should be combined with promizole. Para-aminosalicylic acid in place of promizole or in addition to it may prove to give equal or better results.

Streptomycin has the disadvantages of being neurotoxic and of permitting drug-resistant strains of tubercle bacilli to develop. Toxic reactions may be expected with both streptomycin and promizole. Many of the extrapulmonary and meningeal forms of tuberculosis in children respond remarkably well to streptomycin. Surgical procedures may be made possible or be followed by improved results when preceded by a course of streptomycin. Lives of children with tuberculous meningitis are being prolonged or saved by the use of streptomycin, but final figures await further follow-up.

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Treatment of Chickenpox

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HOYNE

Among the common diseases of childhood, chickenpox usually is regarded by parents as an annoyance rather than as an illness to be feared. There is some justification for this attitude because as a rule the infection is not severe and complications are infrequent. Nevertheless, unforeseen dangers occasionally develop and in some instances may be attributed to neglect or failure to comply with proper instructions. Therefore, in considering treatment the possibility of complications should not be ignored.

Secondary infections brought about by traumatizing the lesions may result in local abscesses or very rarely may lead to septicemia. Impetigo may follow the acute stage of chickenpox. Erysipelas, customarily named as a possible complication, is seldom encountered, but in severe attacks bronchopneumonia may alter the prognosis. Involvement of the appendix is not an extremely rare event. When it occurs it is likely to be at the height of the eruption and perforation often follows. In a single year 8 patients of this kind were admitted at Cook County Contagious Disease Hospital in Chicago. In each instance the appendix had ruptured but operations were performed immediately on 7 of the patients who made good recoveries. The remaining patient had an extensive peritonitis and death ensued soon after entering the hospital.

Other uncommon complications are encephalitis, gangrene of the skin and ulceration of mucous membranes resulting in hemorrhage. Even gangrene of extremities has been reported. And varicella gangraenosa, in which gangrene occurs about the base of the lesions, is occasionally observed and likely to be fatal. In this form of the disease extensive hemorrhages may take place into other tissues of the body.

Because the lesions of varicella often appear on the mucous membranes of the mouth and throat it is perhaps not strange for vesicles to develop sometimes about the glottis or within the larynx. Under such circumstances when an infant or young child is concerned life may be threatened by asphyxiation. A similar situation can follow secondary

FIGURE 1. Chickenpox —second day of eruption. Note profusion of lesions on trunk as compared with face and arms.

infection of lesions leading to massive cellulitis of the neck. In either of these conditions death may be averted only by means of a prompt tracheotomy.

Meningitis and neuritis are extremely rare, but probably the complications least likely to be anticipated are those of the eyes, ears and kidneys. Nevertheless when there are lesions on the border of the eyelids conjunctivitis may be produced, especially after crusts have formed which increase the irritation.

Some dermatologists have maintained that the virus which causes herpes zoster is not the same as the one responsible for chickenpox but it is difficult to acquiesce in that belief. On a number of occasions the writer, like many others, has seen children who had never had chickenpox develop an eruption characteristic of this disease and with the usual incubation period following exposure to herpes zoster. Less often transmission of infection is in the reverse order. Rarely do the two diseases appear simultaneously in the same individual. In the writer's experience an attack of herpes zoster has signified almost invariably that the patient never had chickenpox. It is well to keep in mind the relationship between chickenpox and herpes zoster and isolate the latter as well as the former. This is necessary particularly in any institution which cares for children. Otherwise an outbreak of chickenpox may occur and be difficult to control.

There is no method for active immunization and

measures sometimes adopted for passive immunity to establish immediate and temporary protection are unreliable. Human convalescent chickenpox serum has been used and now gamma globulin is likely to be given preference if passive immunization is to be attempted. Some believe that such measures are of value, but the results are not dependable. If the pregnant woman has chickenpox at the time of delivery the baby may develop the disease as early as eight days after birth.

PRINCIPLES OF TREATMENT

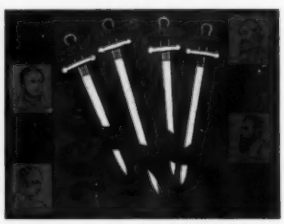
Treatment of the average chickenpox patient is generally a simple affair. But there are certain things which should not be overlooked. The hands should be kept clean and the fingernails cut short. These two precautions will greatly lessen the possibilities of secondary infections. In a very young child it may be necessary to splint the arms or require that white cotton gloves or mittens be worn for a few days. In reality the lesions scarcely ever cause severe itching but a child is likely to pick at the vesicles or crusts. If the eruption is profuse on the scalp it may be advisable to cut the hair as short as possible.

Locally, calamine lotion without the inclusion of phenol is a satisfactory application during the vesicular period. Ointments may be useful after crusts have formed. A good cold cream will serve the purpose if it is desired to hasten the detachment of crusts. However, the longer the crusts remain on uninfected lesions the less chance there is of permanent scars. If the patient has a great many lesions in the mouth a stomatitis may be troublesome and require special attention. Under those conditions a 2 per cent aqueous gentian violet solution may be used with an applicator once a day until relief is obtained. Older children may be given a mild alkaline mouth wash or simply penicillin lozenges.

There is no specific treatment for chickenpox. Convalescent serum and gamma globulin have been prescribed but are not of value. Among the newer antibiotics streptomycin and particularly aureomycin have been tried but neither of these appears to be beneficial. However, the administration of penicillin can always be justified on the theory that it may act as a prophylactic against secondary infections including bronchopneumonia. On such grounds it is probably preferable to give penicillin rather than one of the sulfonamides. However, both drugs may be useful for it should be remembered that most secondary infections of a serious nature are caused by streptococci.

Special measures including blood transfusions may be demanded for some of the infrequent complications to which reference has been made. Encephalitis is treated symptomatically and generally complete recovery takes place within a few weeks. For this condition an oxygen tent seems to be helpful and there is no objection to prescribing aureomycin as well as penicillin. When a chickenpox patient is critically ill the possibility of appendicitis should always be considered. If the appendix is involved the chance for recovery may depend upon an immediate operation.

POSTGRADUATE MEDICINE COVER DEPICTS ATTACK ON CANCER



ALTHOUGH THE PROBLEM of early diagnosis and treatment of cancer has only in recent years become forcibly and dramatically impressed on the public conscience, it has had the best efforts of men and women in every field of medical research and practice for many, many years.

The search for the causative agent or agents of cancer, for reliable diagnostic tests, for effective methods of medical treatment and palliation, for improved surgical procedures, has been pursued slowly but steadily—sometimes marked by a successful advance, more often by disheartening reverses. But most importantly, the search continues—in the laboratories, the hospitals, the great cancer research and detection centers, and always, of course, in the offices of the practicing physicians upon whose skill and judgment depends much of the future welfare of the patient with cancer.

Edmund Kopietz' cover design symbolizes this multifaceted attack against cancer and highlights some of the pioneers whose work has done much to advance the struggle toward a hopeful conclusion.

Reprints of the cover painting mounted and ready for framing are available on request to *Postgraduate Medicine*, 516 Essex Building, Minneapolis 3, Minnesota. $1.00.

Scientific Exhibit

The Control of Cancer in Childhood

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ORIGIN

HEREDITY: The heredity factor in certain tumors of childhood has been long recognized.

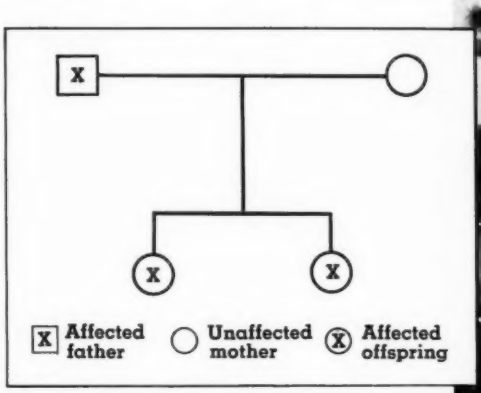


Figure 1. RETINOBLASTOMA.

Figure 2. NEUROFIBROMATOSIS.

Figures 3, 13, 15 and 17 of this exhibit are reproduced from Cancer in Children from Birth to Fourteen Years of Age, by H. W. Dargeon, M.D., J.A.M.A. 136:459-468 (February 14) 1948.

Figure 12 is reproduced from Diagnosis and Management of Neoplastic Diseases in Childhood by H. W. Dargeon, M.D., M. Clin. North America 31:498-524 (May) 1947.

CONGENITAL: The majority of the tumors of childhood are congenital. Although of congenital origin, these tumors may not become clinically evident for a variable period of time after birth. Most hemangiomas appear between the third week and eighth month of infancy. Wilms' tumors and neuroblastomas usually appear between the sixth month and fifth year. Teratomas and Wilms' tumors may not become evident until late adult life.

Figure 3. HEMANGIOMA. Female, age 4 months.

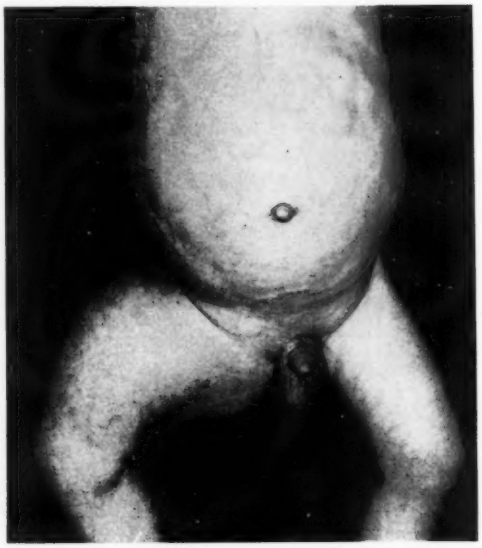
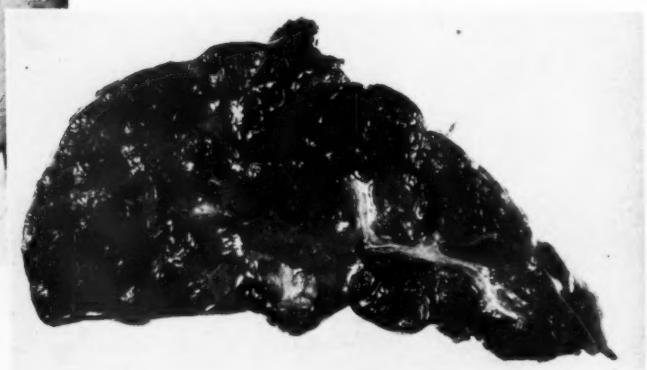


Figure 4. TERATOMA. Male, age 6 months.

METASTATIC: The possibility of metastases from the maternal circulation or extension from a placental implant is strongly suggested in this case of melanoma.

Figure 5. MALIGNANT MELANOMA. Male, age 9 months. Mother died of malignant melanoma three days after patient's birth. Child developed melanoma clinically at 8 months of age.



TREATMENT, PART I

The radical nature of much of the therapy—surgery, irradiation, chemotherapy—requires a careful evaluation of the ultimate as well as the immediate effects of the treatment.

Congenital defects, as well as infectious processes, may simulate tumors. If doubt exists concerning the diagnosis, radical therapy should not be instituted.

TREATMENT, PART II

If a satisfactory result is to be realized, the decisions concerning immediate procedures demand careful evaluation of the *individual* case.

Figure 6. Female, age 7 months. Cystic hygromas may disappear spontaneously. Operation, if necessary, should be deferred in elective cases until 3 years of age.

Figure 7. Male, age 9 years. Malignant alterations in melanoma rarely occur before puberty. Early excision may prevent cancer.

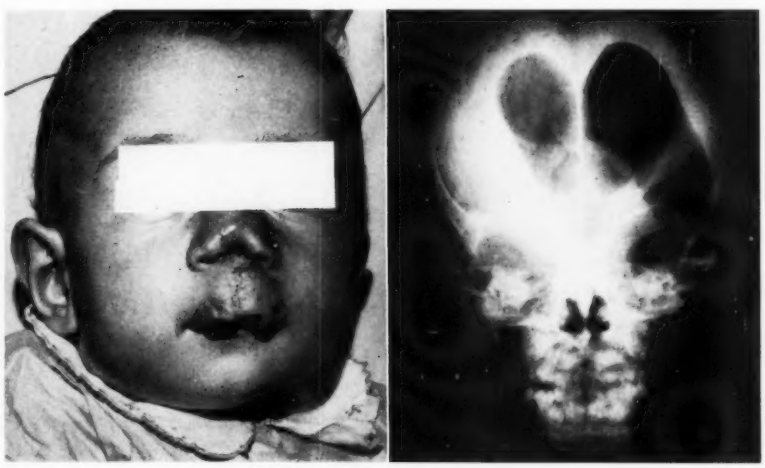
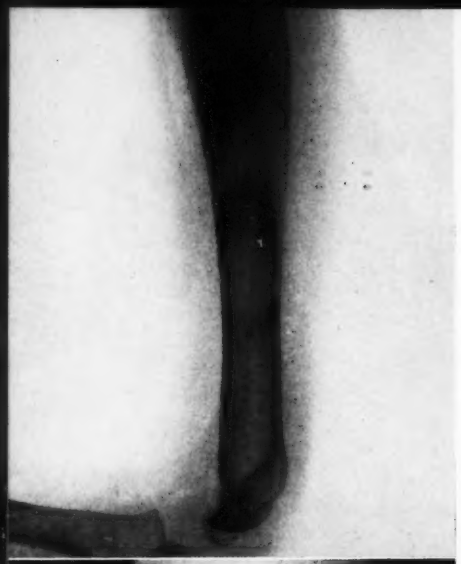


Figure 8. Male, age 16 months. Cerebellar astrocytoma. Observe the child with a tumor for other defects. An occurrence of more than one variety of tumor in the same individual. Hemangioma of the lip.



BIOPSY

Biopsy is a diagnostic necessity in almost all childhood tumors. Exceptions: Retinoblastoma, Wilms' tumors, intracranial tumors. If mass is small, complete excision is preferable to biopsy.

Figure 9. Female, age 2 years. Osteoid osteoma, humerus. Diagnosis prior to biopsy: endothelioma.

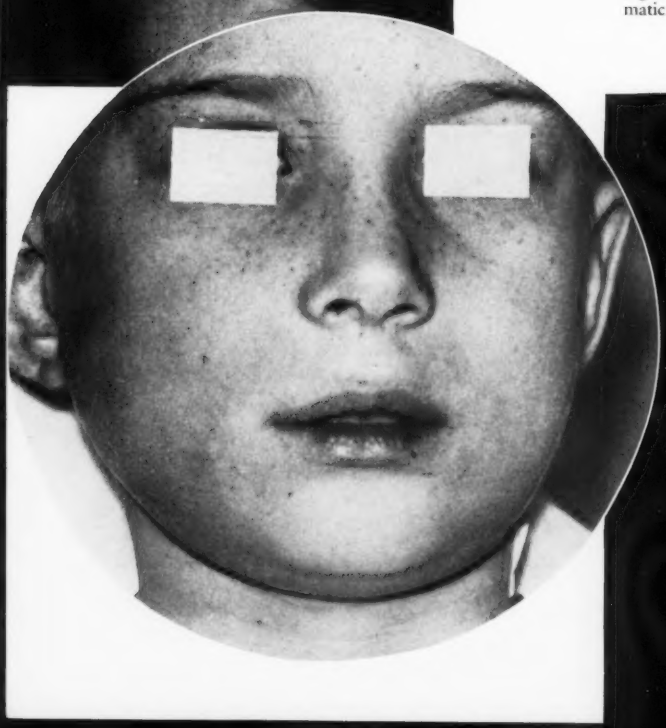
DIAGNOSIS

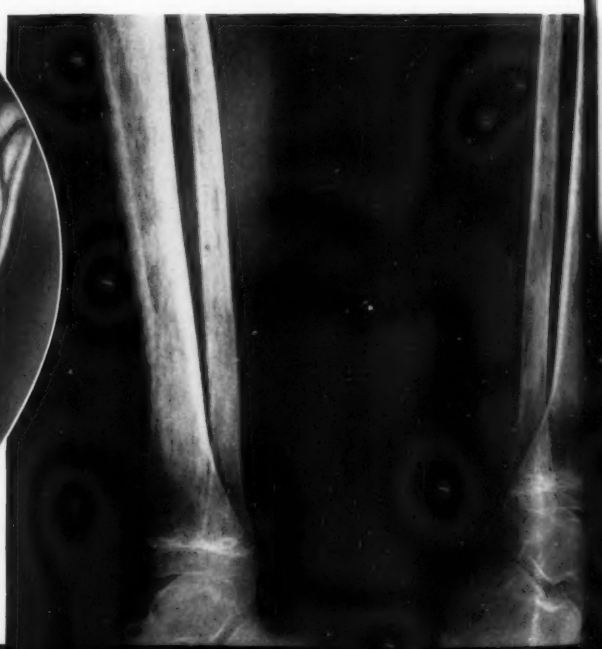
Clinically evident neoplastic disease is never early disease. If recognized, it is either moderately or far advanced.

Figure 10 (left). Female, age 11 years. Osteogenic sarcoma.

Figure 11 (circle). Male, age 7 years. Leukemia. "Swollen glands."

Figure 12 (below). Male, age 11 years. Leukemia. "Rheumatic infections."





DIFFERENTIAL DIAGNOSIS

A presumptive and frequently an exact diagnosis may be made promptly. Neoplasm must be included in the differential diagnosis of any disorder which is:

Chronic, subacute or periodic in character.

Figure 13 (right). Female, age 6½ years. Rhabdomyosarcoma. Tumor of thenar eminence and congenital absence of muscles of left thenar group.

Figure 14 (center). Female, age 3 years. Lymphosarcoma. Presenting some unusual symptom complex. First clinical evidence was unilateral (right) inguinal adenopathy.

PROGNOSIS

The prognosis depends upon the inherent nature of the tumor—a variable—and the adequacy, as well as promptness, of the treatment. These children whose tumors were of serious nature have all survived five years.

Figure 15 (below). Female, age 7 months. Ewing's tumor. Surgical excision; x-ray therapy, 1944. Survival, five years.

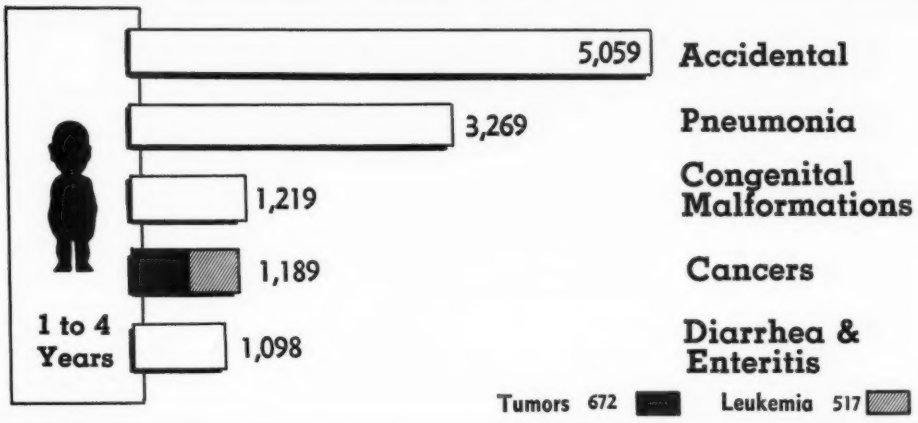
Figure 16 (circle). Female, age 9½ months. Retinoblastoma, bilateral. Surgery, x-ray therapy, 1933. Survival, sixteen years.

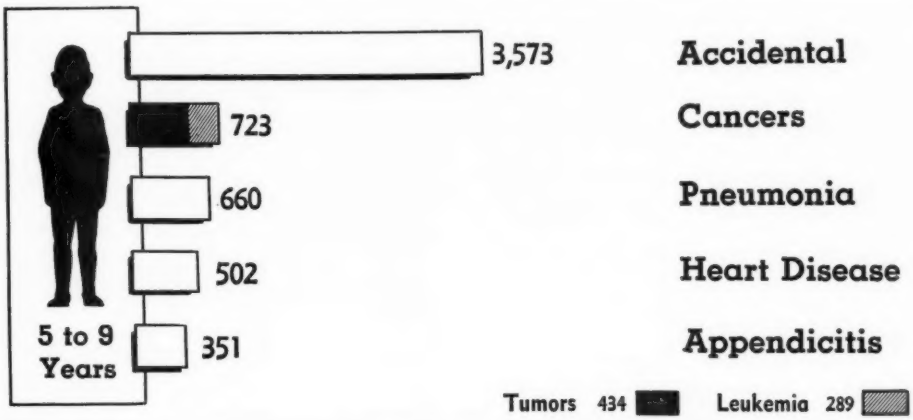
Figure 17. Female, age 12 years. Lymphosarcoma. Radical neck dissection; x-ray therapy, 1940. Survival, nine years.

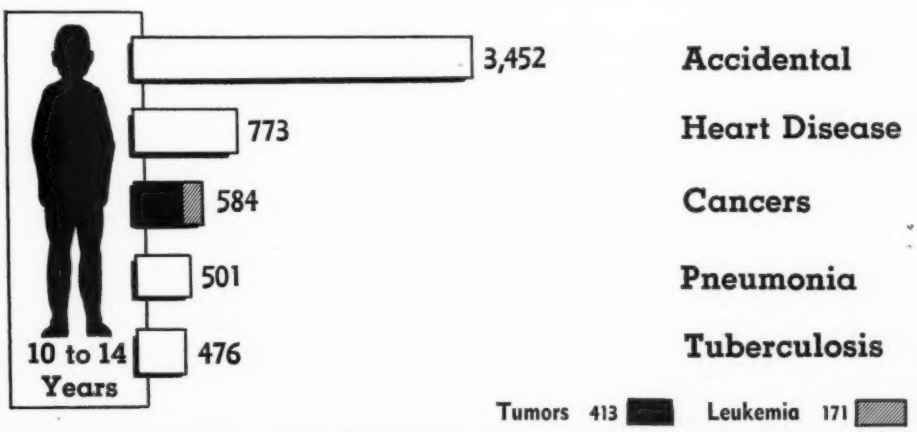
Figure 18 (below). Female, age 2 years. Myxosarcoma. Amputation, x-ray therapy, 1928. Survival, twenty-one years.

Figure 19 (below). Female, age 2 months. Sarcoma, unclassified. Biopsy, x-ray therapy, 1934. Survival, fifteen years.

PRINCIPAL CAUSES OF DEATH IN CHILDREN







Source: U. S. Bureau of the Census. Vital Statistics of the United States, 1945.

GENERAL PRACTICE *Review*

To provide the general practitioner, as well as the specialist with concise, readily available information on the latest, proved methods of treatment of conditions commonly encountered in an average practice, POSTGRADUATE MEDICINE *offers this department to its readers. It is not, of course, intended to present these discussions as the only acceptable therapeutic procedures to be used, but rather to offer simple regimens and recommendations based on the extensive experience of the physicians who prepared these summaries.*

Treatment of Urinary Infections

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THE treatment of urinary infection has advanced considerably in the last decade and is now in such a fluid state that no dogmatic statement can be made.

The first and unchangeable principle is that practically all urinary infections are the result of complete or partial obstruction to the urinary flow. In many instances the location and character of this obstruction are quite evident. In some conditions, however, they are quite obscure, requiring the most complete urologic examinations, such as cystoscopy and pyelographic studies. Obviously, then, the first principle is to locate, determine the nature of, and relieve the obstruction.

The second principle is that no known chemotherapeutic agent or antibiotic is now available which will inhibit or destroy all the organisms commonly causing urinary infections.

The third principle is that there appears to be a selectivity of drugs, certain agents inhibiting certain organisms but not affecting others. Therefore, wherever possible, all organisms causing urinary infection should be identified and the proper drug administered for that particular bacteria.

We have made an effort to determine by test tube and clinical observation which drug is most likely to be successful in a given infection. The results of these studies, in our patients, are the basis of our discussion.

The organisms most commonly encountered in urinary infections, with their incidences, are listed in Table 1.

TABLE 1

PERCENTAGES OF STRAINS ISOLATED IN 150 CASES

ORGANISM	PER CENT
Escherichia coli	28
Pseudomonas	18
Escherichia intermedium	9
Aerobacter aerogenes	9
Proteus	7
Streptococcus fecalis	7
Paracolon	7
Alcaligenes	4
Streptococcus hemolyticus	3
Monilia albicans	3
Staphylococcus aureus	5

Various species within a group have not been listed to avoid confusion and to simplify application of treatment as much as possible. The Escherichia coli is the most commonly seen and the most easily inhibited as a rule. The Staphylococcus albus is often a contaminant. The Staphylococcus aureus is usually pathogenic. The incidence of Pseudomonas, Proteus, and Aerobacter aerogenes will vary in clinics. This will be influenced somewhat by contamination, particularly where instrumentation has been used. This is a strong argument for careful aseptic technic in the performance of all urologic procedures.

In discussing the effectiveness of an antibiotic, it is evident that there are certain strains within a species which are resistant and may persist even

*These studies were made at St. John's Hospital, St. Louis.

though the majority of the organisms may be successfully inhibited. This is quite true of streptomycin and less so of penicillin. It is possible, also, that if an organism is subjected to a sublethal dose, this organism may take on an increased resistance. It is this variation of effectiveness within a species that makes a sensitivity test more accurate than the isolation and identification of the organism alone. Since sensitivity tests are quite technical and many laboratories are not prepared to make them, the knowledge of which drug is most likely to inhibit a certain species isolated is of considerable practical value.

PENICILLIN

A few words should be said about penicillin even though well known by this time. Penicillin fulfills many of the requirements of an ideal antibiotic:

1. It has a high degree of specificity; that is, the group of organisms which it is known to inhibit affects all the strains in that group to a very high degree. This is probably because its action is powerful and not weak.

2. It is low in toxicity, thus permitting overwhelming doses to be given without danger. Allergic reactions occur in about 8 per cent of cases treated, the procaine penicillin G causing less reaction than the penicillin in beeswax. Therapeutic shock, such as the Herxheimer reaction, in the treatment of syphilis due to the sudden release of the toxins from the killed spirochetes, sometimes occurs.

3. It can be administered in many forms because it is active in body fluids and is not destroyed by tissue, enzymes, or pus. The 300,000 or 400,000 units of procaine penicillin G, given once daily, intramuscularly, is the most popular dose since, by this method, it maintains a satisfactory therapeutic level for twenty-four hours. Aluminum monostearate added to the procaine penicillin G is said to maintain a satisfactory therapeutic level for a period of four days.

4. Bacterial resistance is very rare with penicillin and, when present, develops very slowly. It has been demonstrated in Staphylococcus aureus, both in vitro and in vivo, more than in any other organism. Contrasted with this are the sulfonamide drugs and streptomycin which cause the development of bacterial resistance to such a high degree that their usefulness is becoming more and more limited.

Penicillin is most useful in the treatment of coccal infections such as the staphylococcus and streptococcus. It is not very effective against Streptococcus fecalis and Streptococcus viridans. Penicillin is of very little value in the inhibition of gram-negative bacilli which are so common in urinary tract infections. In a mixed infection of staphylococcus or streptococcus with B-coli, the B-coli should be eradicated before using penicillin, since the B-coli develops a penicillinase which inactivates the penicillin. It is more effective in an acid urine.

In the treatment of nonspecific urethritis and prostatitis, it has been somewhat disappointing. Better results have been obtained in epididymitis but its action has been quite unreliable in this. About 60 per cent of the penicillin is excreted in the urine, primarily through the tubules in the first hour after injection. Caronamide has been used to block the renal tubule secretion, but its use has not become popular in the treatment of urinary infections, since it prevents high concentration in the excreted urine.

STREPTOMYCIN

Streptomycin has a field of usefulness not covered by penicillin since it is particularly effective against gram-negative bacilli. Its greatest drawback is its tendency to cause bacterial resistance both in vitro and in vivo. This resistance is developed very promptly, appearing sometimes in twenty-four hours and to a very high degree. For example: A bacillus of the Escherichia coli group, which originally was inhibited by 1/10 of a micro unit per cubic centimeter, after exposure to a sublethal dose for twenty-four to forty-eight hours, may develop a resistance in some instances of 250 micro units or even 1,000 micro units. This resistance, when once acquired, never changes with time or other influences. It is readily seen how serious this becomes, when no other agent is available to combat these resistant organisms.

Fortunately, other antibiotics, such as aureomycin and chloromycetin will inhibit a certain number of these acquired resistant forms. Streptomycin, also, has its limitations, in that it will fail to inhibit some strains within a given group. For example: It will inhibit 20 per cent of the organisms identified as Pseudomonas yet fail to inhibit 80 per cent of this species (Table 2).

TABLE 2
STREPTOMYCIN SENSITIVITIES

ORGANISM	STREPTOMYCIN SENSITIVE, PER CENT	STREPTOMYCIN RESISTANT, PER CENT
Gram-negative bacilli, all types	56	44
Escherichia coli	95	5
Pseudomonas	20	80
Escherichia intermedium		100
Aerobacter aerogenes	62	38
Proteus	73	27
Paracolon	40	60
Alcaligenes	17	83

Penicillin, on the other hand, has the quality of

being effective against practically all of the strains within a species. This shortcoming, noted in streptomycin, makes it necessary not only to identify the organism but also to determine its sensitivity. A large, overwhelming dose to avoid a sublethal dose would be advisable except for the fact that the margin of safety of streptomycin is considerably less than that of the other antibiotics. Toxicity often develops when the usual dose is merely doubled; therefore, the dosage must be handled more carefully than with other antibiotics.

The toxicity of streptomycin is well known. The most common reaction is impaired function of the vestibular portion of the eighth cranial nerve. It is serious since it is often permanent, only compensated for by a visual correction. Toxicity usually develops as the result of large doses given over a long period of time. It may be said that the administration of streptomycin may be discontinued in the treatment of urinary infections if results are not obtained in six days. Dihydrostreptomycin apparently causes less toxemia and is especially recommended in prolonged treatment such as endocarditis and tuberculosis.

The indiscriminate use of streptomycin is condemned for the reasons given and should be used in patients with low kidney function with considerable caution since a high blood level may be built up. Streptomycin should be administered in the presence of an alkaline urine since its effectiveness is increased three- or fourfold.

AUREOMYCIN

Aureomycin, first described in July, 1948, bids fair to be of widespread usefulness in the treatment of urinary infections. It is readily absorbed when given by mouth, appearing in the blood in about thirty minutes, with maximum concentration in the urine between two and eight hours following a single dose. The usual concentration of aureomycin in the blood is from 2 to 4 micrograms. Although intravenous and intramuscular injections are possible, due to its high acidity it is quite irritating; also, it is quite unstable. The oral dosage ranges between 25 to 100 mg. per kilogram of body weight. We have administered 2 capsules (¼ gm. each) every six hours, as a routine treatment. A much larger dose may be given when resistant strains are present. A higher concentration is not always obtained in this manner.

Aureomycin is much more active in an acid medium. Bacterial resistance has not been noted by us or other workers to a high degree to date. We observed it in only one instance in vivo and in vitro.

The toxicity of aureomycin is very low. No allergic reactions have been noted and no blood dyscrasia. Nausea and diarrhea were present to some degree in about 15 per cent of the patients. This is somewhat alleviated by the administration of aluminum hydroxide or buttermilk and disappears promptly following withdrawal of the drug. A more refined product, recently studied, suggests that this annoying feature may be eliminated. Although useful in some coccal infections, its greatest value is found in the treatment of bacillary infections. Nonspecific urethritis, prostatitis, and Reiter's disease are favorably affected by aureomycin, suggesting that the drug may be useful against virus infections.

Urine that is culturally clear during the administration of aureomycin has been found to become positive after discontinuance of the drug. This may be due to the fact that the concentration of aureomycin in the tissue may be considerably less than the concentration in the urine and not sufficient to destroy all infections in the body but sufficiently concentrated in the urine to cause inhibition on culture. It is, therefore, suggested that the aureomycin treatment be continued for some time after the negative culture is obtained. The greatest value of aureomycin has been against those organisms which have been resistant or developed resistance to streptomycin.

In our series of 72 organisms, the in vitro studies indicated that Escherichia coli, Escherichia intermedium, Aerobacter aerogenes, Paracolon, Alcaligenes, and Streptococcus fecalis are sensitive to aureomycin in concentrations which can be obtained easily in the body. Detailed studies are tabulated in Table 3. The blood level should be three or four times that which inhibits the organism in the test tube. The clinical course fairly well parallels the experience indicated by the in vitro studies as indicated by Table 4.

TABLE 3

AUREOMYCIN SENSITIVITY RANGE

ORGANISM	SENSITIVITY RANGE *Micrograms/cc.*
Escherichia coli	0.6 to 0.15
Pseudomonas	2.5 or more
Escherichia intermedium	0.3 to 0.07
Aerobacter aerogenes	0.3 to 0.07
Proteus	2.5 or more
Paracolon	0.6 to 0.02 or less
Alcaligenes	0.6 to 0.07
Streptococcus fecalis	0.07 to 0.02 or less

CHLOROMYCETIN

This most recent antibiotic inhibits the growth of many bacteria in very high dilution, requiring as little as 0.1 microgram to be effective. It is quite stable, relatively insoluble in water, but readily soluble in the gastrointestinal tract. It is a neutral compound. When taken by mouth, it appears in the urine quite promptly. It is the first antibiotic

TABLE 4

RESULTS OF AUREOMYCIN TREATMENT GROUPED IN RELATION TO ORGANISMS

ORGANISM	NUMBER OF CASES	SENSITIVITY RANGE *Micrograms/cc.*	CULTURE *No growth*	CULTURE *Growth*
Aerobacter	6	0.3 to 0.15	4	2
Intermedium	10	0.15 to 0.07	9	1
Escherichia coli	6	0.6 to 0.3	6	0
Paracolon	6	0.3 to 0.15	6	0
Streptococcus fecalis	8	0.07 to 0.04	8	0
Pseudomonas	8	2.5 or more	2	6
Proteus	4	2.5 or more	0	4

to be chemically analyzed successfully and a synthetic preparation made. When this can be done on a commercial scale, it will, no doubt, reduce the cost of production considerably. Chloromycetin is nontoxic in very large doses and is well tolerated over a long period of time. The usual dose is ¼ gm. capsule every four hours.

Our studies indicate that it has a very broad range of usefulness in bacillary infections. The in vitro studies show that small concentration of the drug inhibits most of the bacillary infections found in the urinary tract. The most resistant organisms seem to be the Pseudomonas and Proteus.

The results of sensitivity tests made in our laboratory are expressed for clarity in percentage of inhibition in concentrations which can be attained in vivo (Table 5).

TABLE 5

SENSITIVITY TESTS WITH CHLOROMYCETIN

ORGANISM	NUMBER OF ORGANISMS	PERCENTAGE OF INHIBITION
Escherichia coli	8	87
Escherichia intermedium	5	80
Aerobacter aerogenes	10	70
Paracolon	3	100
Proteus	7	50
Pseudomonas	11	0
Streptococcus fecalis	4	0

The in vivo studies have been somewhat confusing to date and are not yet sufficiently clearly defined to justify any positive statements concerning its usefulness in any given organism. It would appear that it is effective against Escherichia coli, Paracolon, Intermedium, Aerobacter aerogenes, and less useful for the Proteus. We have not found it effective against Pseudomonas.

GANTRISIN (NU-445)

Gantrisin is a sulfonamide which has a high solubility over a wide *p*H range. This is a valuable consideration because it is less toxic and does not form concretions as do other sulfonamides.[1] This property permits it to be given in high concentration (4 gm. in 10 cc.) intravenously or intramuscularly. It also permits administration of the drug without concomitant alkali or forced fluids.

A number of reports on NU-445 in the treatment of urinary tract infections have appeared.[2-8] These reports in general confirm the manufacturer's claims regarding the high solubility and low toxicity. Sarnoff,[2] for example, reported that 3 gm. of NU-445 were given every four hours for ten days without any reactions.

We endeavored to make a careful study of the sensitivity of various organisms to NU-445 as determined in the test tube and to correlate these findings with our clinical experience.

The results would indicate that this new drug is effective in urinary infections when due to Escherichia coli, Proteus, and Alcaligenes. It is the drug of choice in Proteus infections since the Proteus is not highly sensitive to any of the antibiotics. It was found to be effective in infections which had become resistant following streptomycin therapy. The Aerobacter aerogenes, Paracolon, and Intermediate organisms responded fairly well to NU-445. The Streptococcus fecalis and the Pseudomonas were highly resistant, both in sensitivity tests and clinical trial.

The attractive feature of the drug is that it can be given by mouth and is apparently nontoxic in required dosage. It is well tolerated by the patient. The usefulness is broadened by the fact that its high solubility permits intravenous and intramuscular injections also. Gantrisin is available as a 40 per cent solution of the diethanolamine salt in ampule form. Four grams are contained in 10 cc. ampules which can be injected intravenously at one time without toxic effect. It may be described as a sulfonamide with low toxicity, high solubility, and particularly effective in Proteus infections.

NU-445 is now available commercially under the trade name GANTRISIN.

MANDELIC ACID

A discussion of the treatment of urinary infections would not be complete without some statement concerning mandelic acid. Before we had

antibiotics, mandelic acid was by far the most effective urinary antiseptic. In the form of mandelamine, which is a combination of methenamine and mandelic acid, it continues to be a valuable urinary antiseptic. It is nontoxic, well tolerated, and easy to administer. It is effective in a high percentage of organisms found in the urinary tract, provided the urine is maintained in an acid state. It will not act in an alkaline urine and, therefore, all alkalies in the form of drugs or food should be prohibited during its administration. It does not cause the development of increased resistance as does streptomycin. We have found it effective against many strains of Aerobacter aerogenes and Pseudomonas which were highly resistant to all other forms of therapy.

A concentration of 1 per cent mandelic acid must be maintained in the urine and in order to obtain this, at least 12 gm. of mandelic acid must be given by mouth. Four tablets of mandelamine, given 3 times a day, will accomplish this.

The most resistant organism we have is the Pseudomonas and as yet we have no chemotherapeutic agent which will eliminate all of its strains.

Table 6 is given as a suggestion of the chemotherapeutic agents to be used in the various organisms identified as causing urinary infections.

No rules or charts can take the place of judgment which is necessary in the treatment of each patient. Streptomycin, for example, may be used in practically all of the bacillary infections and has been found effective in at least 55 per cent.

Mandelamine is used by us in many types of infection, particularly in patients who are not to be under our constant observation, such as postoperative urinary calculi patients and patients who have undergone prostatic surgery.

It is obvious that all physicians may not have access to a bacteriologist who can isolate and identify the infecting organism. Every effort should be made under these circumstances to obtain such facilities, since the effort will be well repaid by obtaining favorable results in otherwise chronic and unfavorable conditions.

TABLE 6
SUGGESTED TREATMENT

ORGANISM	DRUGS OF CHOICE
Escherichia coli	Gantrisin (NU-445) Aureomycin Chloromycetin Mandelamine
Escherichia intermedium	Aureomycin
Aerobacter aerogenes	Aureomycin Chloromycetin
Pseudomonas	Streptomycin (20 per cent effective)
Proteus	Gantrisin (NU-445)
Paracolon	Chloromycetin
Alcaligenes	Aureomycin
Streptococcus fecalis	Aureomycin Mandelamine
Streptococcus hemolyticus	Penicillin
Staphylococcus aureus	Penicillin

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Herpetic Lesions of the Oral Cavity

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The treatment of oral herpetic manifestations can be divided into the treatment of (1) the solitary or sporadic aphthous ulcer, (2) acute herpetic stomatitis, and (3) recurrent herpetic stomatitis.

The application of caustics such as 50 per cent trichloracetic, liquefied phenol, or 10 per cent silver nitrate to the sporadic aphthous lesions will temporarily minimize the pain. The patient can repeatedly touch the lesions with an ordinary alum

styptic pencil at frequent intervals.

In patients with acute herpetic stomatitis, a warm sodium bicarbonate mouthwash (1/2 teaspoon sodium bicarbonate to 2/3 glass of warm water) is well tolerated by the tissues, and aids in reducing the oral flora and removing the mucous debris. The application of any nonirritating antibacterial or antibiotic agent such as tincture of metaphen, 2 per cent aqueous crystal violet, or topical penicillin will reduce the oral flora and lessen the pain.

Aureomycin, 250 mg. every three hours, is very effective in controlling the pain in acute herpetic stomatitis.

High therapeutic doses of vitamin B complex and vitamin C (6 to 9 therapeutic capsules per day) should be administered for two or three days, after which the dosage can be gradually reduced. Vitamin B complex therapy seems to shorten the duration of the acute symptoms. The patient should be encouraged to consume a liquid or soft diet. Fruit juices cannot be tolerated, but malted milk, eggnogs, and ice cream can usually be eaten. Caustic agents are contraindicated in acute herpetic stomatitis.

The acute recurrences of herpetic stomatitis are treated as described previously; however, the patient is more interested in measures which can be taken to prevent future attacks. The patient should be questioned about known food allergies which might serve as predisposing factors. In the event a negative history is obtained relating to food allergy, repeated vaccinations with smallpox vaccine should be tried.

The course should consist of 8 to 10 vaccinations, performed at seven- to ten-day intervals. The vaccinations should be continued regardless of whether a "take" is obtained. Following the initial vaccination, a flareup of the oral lesions may occur and the patient should be warned about this possibility. For the same reason it is unwise to begin vaccination therapy during a period when acute lesions are present in the mouth. If the patient fails to receive benefit from the first course of vaccinations, a second series is worth trying.

If vaccination therapy fails to result in improvement, complete allergic studies should be made. Foods to which the patient is found to be sensitive should be eliminated from the diet until it is determined whether they are the cause of the recurrent stomatitis.

If allergic causes are not believed to be responsible for the recurrent herpetic stomatitis, sex hormone therapy may be tried in an attempt to cause increased keratinization of the oral mucosa which will render this tissue less susceptible to the herpes virus. Estrogen therapy can be employed as an ointment locally or parenterally. If the ointment is used, approximately 25,000 rat units per week are recommended, with 1,000 rat units per gram of ointment. Systemic reactions are less likely to occur with the local application of estrogens.

About 20 per cent of the patients with the recurrent form of this disease do not respond to any of the methods of treatment indicated.

Lymphedema of the Extremities

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The treatment of lymphedema of the extremities remains a complex problem despite the recent accumulation of experimental and clinical evidence of its etiology and pathology. Lymphedema develops from a variety of causes. That due to cardiac or metabolic disorders will not be considered here but must be differentiated from that due to local causes.

Mechanical obstruction of the lymphatics due to filariasis, carcinoma, postradiation fibrosis, or recurrent inflammation, usually streptococcal, may produce chronic edema.

Thrombophlebitis may produce secondary inflammation of the perivascular lymphatics and consequent edema.

Incompetent valves in the veins of the legs may increase capillary pressure or alter capillary permeability with resulting edema.

Finally, the edema in the lower legs, described by Milroy, which usually develops at puberty, can be explained only on a hereditary basis because neither venous nor lymphatic obstruction is demonstrable.

A method of experimental production of chronic lymphatic obstruction in animals devised by Drinker, Field, and Homans in 1934 is the basis for our present understanding of the changes in the tissues which occur during the development of lymphedema. They described an early transient pitting edema followed by a permanent, brawny, indur-

ated swelling of the leg indicative of beginning irreversible fibrosis. With continued fibrosis, the resulting picture is one of typical elephantiasis. The tissues show grossly dilated lymphatic trunks with thickened skin and subcutaneous tissue and microscopic evidence of marked fibrosis. The lymph recovered from these tissues contains an abnormally high percentage of protein.

Increased tissue susceptibility to infection was observed in the experimental animal just as is observed clinically. Spontaneous development of diffuse infection has been observed and hemolytic streptococci have been grown from the lymph removed in the early hours of the attack. Each episode of infection merely intensifies the permanent changes in the tissues.

GENERAL MEASURES

The general measures in the case of a patient with chronic lymphedema should be directed toward avoiding infection and prolonged dependency of the part. Because of the increase in local tissue susceptibility and the danger of accelerating the permanent changes, active foci of epidermophytosis or other foci of infection should be eliminated to minimize the risk of precipitating an episode of local inflammation. With recurrent infection, it would be desirable to recover the organism for virulence and sensitivity studies. However, even without this evidence, sulfonamides or antibiotics should be administered empirically to control the inflammation which usually is caused by a beta hemolytic streptococcus. Prolonged dependency exaggerates the edema by increasing hydrostatic pressure and reducing the ability of the lymphatics to empty themselves of the stagnant lymph.

The milking action of the muscles of the legs should be aided by support of the part either with an elastic bandage or an elastic stocking extending from the toes to above the knee. As much rest and elevation of the extremity as possible is desirable to drain the congested lymphatics. The fact that most patients observe considerable reduction in swelling on arising in the morning is indicative of the degree of mobility of the lymph in the swollen extremity.

SPECIFIC THERAPY

Specific therapy depends on the causes of the lymphedema and the degree of the permanent changes that have occurred in the lymphatics and surrounding tissues. If the edema fluid can be mobilized and the cause of its collection eliminated, as for example in venous congestion of the leg, the lymphedema may be successfully controlled. In others, as in Milroy's hereditary edema, the permanent changes may progress despite treatment.

The lymphedema which is a sequel to deep thrombophlebitis of the extremity is often reversible if the elevated pressure in the veins of the legs can be reduced. Recanalization of the thrombosed vein may result in permanent damage and incompetence of the venous valves. Adequate restoration of the venous circulation can best be accomplished by surgical interruption of the incompetent canalized venous system. Linton has described an operation consisting of ligation and stripping of the saphenous veins and division of the femoral distal to the profunda femorus vein. He reports that the edema has subsided in the majority of cases.

If the obstruction is mechanical, certain bypassing procedures have been suggested to establish collateral lymphatic circulation. These are based on the well recognized regenerative power of the lymphatic system.

The edema of the arm, which may follow a radical mastectomy, can be reduced by attaching the upper arm to a flap of skin and subcutaneous tissue from the chest wall. The motions of the arm will of necessity be limited by the procedure but the relief of the edema may justify the disability.

For the leg, a flap of skin and subcutaneous tissue based above Poupart's ligament can be rotated from the abdominal wall across the groin to the upper thigh and may serve as a bridge for the escape of edema fluid from the lymphatics of the leg into the lymphatics of the abdominal wall. However, the procedure in the leg is not as generally successful as that in the arm, although successful results have been reported.

The above methods of treatment are valuable if a considerable proportion of the swelling consists in fluid which can be drained away. They are of little use after extensive permanent fibrosis has developed.

It is in patients with irreversible changes that the surgeon meets his greatest challenge, for palliation is no longer successful and relief is possible only by radical excision of the diseased tissue. In these cases the skin is greatly thickened and thrown into irregular folds and projections. The dermis and subcutaneous tissues are thickened and fibrotic with numerous pockets of lymph throughout. On the outer surface of the thickened deep fascia large pools of lymph are present. By contrast, the under surface of the deep fascia and the underlying muscle appear normal.

SURGICAL TREATMENT

The Kondoleon operation (1912), one of the earliest methods of surgical treatment, has a twofold purpose: (1) to reduce the size of the leg by removing the thickened tissue, and (2) to allow drainage from the damaged superficial lymphatics into the normal deep lymphatics.

The operation in two or more stages is done

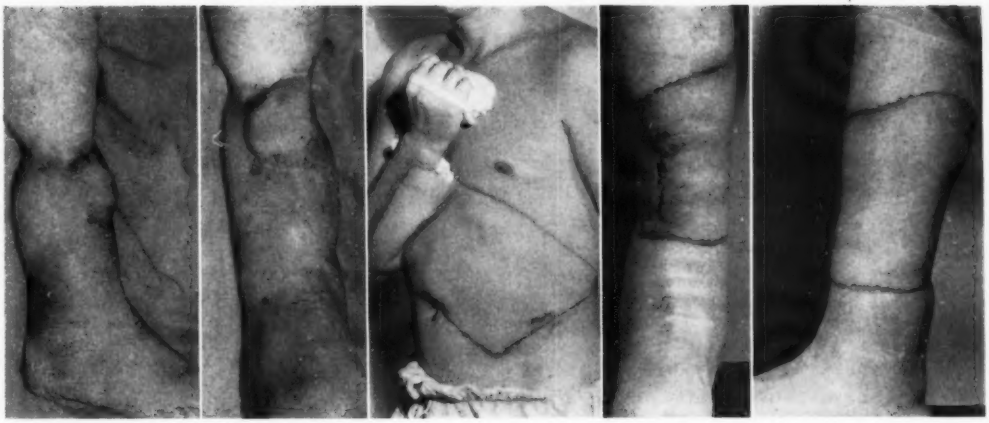

FIGURE 1. Chronic edema of the right lower leg due to congenital constriction ring about the mid-calf with resulting recurrent attacks of lymphangitis and cellulitis of the foot and lower leg. Circulation of the foot corrected and edema reduced by sleeve excision of the constricting band and covering the circumferential raw surface with an open jump flap from the abdominal wall, carried on the forearm. The narrow flap visible anterior to the tibial crest had been unsuccessful in relieving the lymphedema. Residual edema from permanent fibrosis in the subcutaneous tissues of the foot persists, but has become less than that shown in the final photographs. No recurrence of lymphangitis or cellulitis.

through an incision on either side of the leg. The skin is reflected as anterior and posterior flaps, allowing access to the thickened subcutaneous tissue and deep fascia which are then widely excised. The skin flaps are replaced directly on muscle and closed loosely after excision of the excess skin. Success depends on the patency of the remaining lymphatics but removal of a part of the thickened mass is in itself beneficial.

Multiple stage excision of all the diseased tissue and repair by skin grafts is a more difficult procedure but one which offers more complete relief. All cutaneous and subcutaneous lymphatics are removed and lymph drains through the deep lymphatics. For this reason the excision should include the skin, subcutaneous tissue, and deep fascia of the dorsum and sides of the foot. Although not present as early as in the legs, the fibrotic thickening of the tissues of the foot may occur following the excision of the subcutaneous lymph channels proximal to the foot. Primary excision of this tissue is easier than after the late permanent changes have developed.

If the skin of the diseased leg is smooth, split skin grafts from it may be used. If unavailable, skin must be secured from the trunk or possibly upper thighs. In any case, a large area of skin is needed to cover even the reduced circumference of the leg.

Primary healing with a minimum of infection is essential to success in either the Kondoleon or the skin grafting procedure. To prevent the accumulation of lymph or blood beneath the skin after operation, a firm pressure dressing is applied from toes to midthigh. The first change of dressing is done in five or six days, and a similar dressing reapplied. The frequency of subsequent dressings is determined by the condition of the skin flaps or grafts, but must not be discontinued until the skin is well healed.

Motion of the leg muscles may be started after several weeks when the danger of dislodging the skin is past. A supporting bandage or elastic stocking must be worn by the patient for at least a year and often permanently. Prolonged standing should be avoided. Hygiene of the feet, especially the skin between the toes, is most important in avoiding infection.

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EDITORIALS

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THE ETHICAL BASIS OF MEDICAL PRACTICE

Dean Willard L. Sperry of the Harvard Divinity School has elaborated some lectures on medical ethics given in the Massachusetts General Hospital and in the Medical School of the University of Michigan into a book, entitled "The Ethical Basis of Medical Practice."* Dr. J. H. Means is pleased with the book and calls attention to the overlapping between the ministerial profession and medicine. He believes, however, that Dean Sperry has been "overgenerous to my profession. The doctor may be worthy of this praise individually, but when he organizes he falls far short of it." Notwithstanding that such comment may deter many physicians from reading Dean Sperry's book, the work itself is well worth any doctor's time.

Far too few worth-while books concerned with the philosophic aspects of medical practice are available. The broad concept of medicine held by Dean Sperry will be inspirational to many general practitioners. His emphasis on the personal relationship between doctor and patient will warm the hearts of all of those who distrust mass medicine.

Dean Sperry recognizes the difference between a profession and a trade. He recognizes the difficulty of assessing fees: "One does not see how there can be anything like a fixed charge for a heavy operation, particularly when it is of a critical and difficult nature. . . . A transaction of this sort is not a matter of mere lapse of time over an operating table."

Many a medico is going to be happy also over Dean Sperry's comments on what is commonly called socialized medicine. The accuracy of the Dean's observations entitles him to a scientist's standing. He recognizes that socialized medicine already prevails in the wards and outpatient departments of many of our hospitals. He recognizes also that Aneurin Bevan has undoubtedly overbid his hand and has already had to stage two or three strategic retreats in the interest of necessary economies. He continues that "in far too many instances under socialized medicine a doctor's practice will become an assembly-line process, rather than a handicraft." Dean Sperry is convinced that once these systems prevail, the best type of men will not go into medicine as a profession. Indeed the conclusion merits complete quotation:

> "One can only say that the future of socialized medicine would seem to depend upon the ability of the state to inspire in its doctors an unflagging idealism which can stand the wear and tear, as well as the financial restrictions, of a regimented practice under such conditions. England fortunately for herself has a well-rooted tradition of public service in advance

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of anything which obtains in this country. We shall need a new birth of patriotism and of our conception of citizenship before socialized medicine here can deliver that which it promises. Not that the American doctor is lazy or selfish, but rather that he likes to be master of his own times and comings and goings. Such is his professional heritage from our historic culture."

With high praise for codes of medical ethics, Dean Sperry proceeds to an analysis of the workings of these principles. He contrasts democratic with totalitarian medicine, leaning heavily on A. C. Ivy's report of what happened to Germany's medical profession.

Later chapters concern the prolongation of life, euthanasia and reverence for life. Medicine needs far more sincere, philosophical contributions like that with which Dean Sperry has provided us.

MORRIS FISHBEIN

HUMANISM AND THE AGE OF SCIENCE

DR. JOHN F. FULTON, Sterling Professor of Physiology in Yale University, gave the Ludwig Mond Lecture at the Manchester School of Medicine on October 6, 1949, choosing for his topic "Humanism in an Age of Science." Hailing Sir William Osler as one of the foremost humanists of his generation and calling attention to a lecture delivered by Osler in May, 1919 with the title "The Old Humanities and the New Science," Doctor Fulton recognized the alarm of those in the humanities over the growing prominence of the sciences. Our universities find it easier to obtain funds for basic sciences or medical research than for the humanities. Doctor Fulton's alarm is occasioned by his observation that science teaching is becoming inferior because many of those who teach science have not had the benefit of a humanistic education. As a mechanism for bridging the gap between the humanities and the sciences, Doctor Fulton recommends the historical approach to the sciences.

His lecture is exceedingly practical in its illustrations of methods by which the historical approach may be employed in teaching. He considers the development of the telescope and traces the various contributions which led to the work of Galileo. The excellent documentation of this section of Doctor Fulton's address is in itself a model for this type of historical research.

Doctor Fulton opens the third section of his essay with a paragraph which deserves earnest consideration by all scientists at this time:

> "The turn that events have taken during recent weeks prompts us to view more soberly than ever the obligation of educated people in the difficult task of earning and maintaining world peace. Never before has a knowledge of the methods of science been so imperative for people in many walks of life—for legislators, reporters, educators, and writers. And never before has the scientist so needed the broadening influence of studies outside his own technological field. Thus, how the sciences and the humanities may be integrated in a truly liberal programme is a question of great import at the present time."

The Ludwig Mond Lecture should be read by everyone interested in medical history and especially carefully by those who teach the medical sciences. We need integration of medical history with teaching in both basic sciences and clinical medicine. Students should be familiar with original writings. They will find in the book by Dr. Ralph Major, "Classical Descriptions of Disease," an easily available source for much of the finest and most important writing in medical science.

MORRIS FISHBEIN

BASIC FACTORS IN SCIENTIFIC RESEARCH

LAST year I had lots of fun writing an article on "Basic Factors in Scientific Research," which I based largely on the autobiographies and biographies of many scientists who had achieved distinction for their contributions to the advancement of medicine. I found that Professor J. B. S.

Haldane considered fundamental to much research the design and perfection of apparatus for observation and measurement.

The extension of medical knowledge that has resulted from the invention of the watch, the manometer, the stethoscope, the ophthalmoscope, the laryngeal mirror and the electric light is so vast as to be incalculable. Amazing results followed the invention of culture media, the electrocardiograph, the kymograph and the innumerable scopes for observing various portions of the human body. A few radioactive isotopes and a Geiger counter can make any man a research worker.

Dr. Walter B. Cannon considered that the experimental method required ingenuity and skill in contriving appropriate devices to secure evidence. In listing the traits important for a career of investigation, Professor Cannon included curiosity, imaginative insight, critical judgment, thorough honesty and retentive memory, patience and good health. Sir James Mackenzie deprecated the student who made progress on the basis of a good memory and urged greater recognition for those with reasoning power. Ramon y Cajal mentioned particularly his belief that the worker must find interest, joy, excitement, pleasure or emotional release in his task. Boredom in the course of investigation would be a fatal toxin.

Much is to be said for hunches but, obviously, much more can be said for the type of man who can evaluate previous evidence, develop a concept and organize the necessary experiments to establish the truth.

A study of the existing evidence puts freedom first—freedom for an inspired individual to pursue his will-of-the wisp wherever chance or fortune may lead him. Harvey Cushing said, "Opportunity, personality, position, chance, in addition to vision and the prepared mind—all have a hand."

Many scientists have written to me following the publication of the article. I have taken a special pleasure in a note just received from Dr. Torald Sollmann, emeritus professor of pharmacology and materia medica, Western Reserve University in Cleveland. Doctor Sollmann says:

> "The first essential for research, I believe, is the joy of doing it. Without that, it is not likely to amount to much.
>
> "Then comes the equipment—temperamental, intellectual and physical. With limitations in any of these, the results must be correspondingly limited—though they may happen to be important.
>
> "Next comes 'liberty'—and an atmosphere of kindred spirits helps a lot.
>
> "Finally, for 'big' results, either intuition, or plain luck.
>
> "Most of us, however, have to be content with our inner satisfaction, with the pleasure of the chase; and perhaps console ourselves with the thought that it takes a lot of fiddlers to produce one violinist."

MORRIS FISHBEIN

CONFUSING THE PARENTS

Pity the poor parents of our modern days who are confronted with a mass of conflicting advice from a variety of sources on what to do with the growing child. Dr. Leo Kanner,[1] associate professor of psychiatry and pediatrics and director of the Children's Psychiatric Service in the Johns Hopkins University, offers a book called "In Defense of Mothers," with the subtitle "How to Bring Up Children in spite of the More Zealous Psychologists." He pleads for common sense and warns parents against expecting the worst.

If the child is placid and good-natured, he may be unduly submissive; if he is active and gets into things, he may become unduly aggressive. One "expert" has set up a new series of the ages of man which begins with the sucking stage, in which he becomes fixated; the child's life is crippled by excessive submissiveness, passivity and masochism. Then comes the biting stage and if the child gets fixated at that point, he emerges as an aggressive, bullying, sadistic person. Finally, someone suggested to a worried mother that the sucking and biting stages were logically followed by the swallowing stage and that if a person reaches

that stage and becomes fixated, he swallows everything he hears.

A recent conference on emotional health, held in Syracuse, New York, offered a variety of views by a number of authorities. Dr. David Rapaport, research associate at the Austin Riggs Foundation, suggested that we stop teaching the philosophy that everyone is created equal and begin to believe that each one has equal rights which are qualitatively different from those of anyone else. Doctor Rapaport said that parents should not treat children as their equals and that frustration is an indispensable part of growing up. Dr. Bela Mittelmann, professor of medicine, New York University, warned parents of gifted children against exploiting the child's talents. He warned particularly about exploiting children in the field of music by getting them to play difficult pieces.

Then Dr. William Cruickshank, director of education of exceptional children in Syracuse University, pointed out that there were more than 12 million children in this country who could be termed exceptional by reason of physical or emotional characteristics and who needed special care, education and treatment. I have estimated that the minimum amount of attention required from competent psychiatrists would seem to require a psychiatrist for every five children or approximately two million psychiatrists just to guide the little virtuosos into proper paths.

We seem to be in the chaotic stage of creation as far as our knowledge of child psychology and what to do about it is concerned. We are, in fact, in the period of early experimentation and few conclusions based on adequate evidence can yet be accepted.

MORRIS FISHBEIN

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JOHN MORRIS DODD
(1866—1950)

DR. DODD

SURGEON; humanitarian; distinguished citizen; Trustee, Interstate Postgraduate Medical Association, 1922-1950; born in Waynesburg, Pennsylvania, on October 5, 1866; M.D., Starling Medical College, Columbus, Ohio, 1889; D.Sc., Northland College, 1925; began surgical practice in Ashland, Wisconsin, 1889; active in city beautification, hospital building and medical development; surgeon to St. Joseph's and the Ashland General Hospitals; founder and President of the Ashland Clinic; President of the Ashland General Hospital Association; Mayor of the City of Ashland, 1911-1913 and 1933-1939; Dodd Gymnasium, the city's largest gathering place, was named in his honor by popular vote; Secretary of the Wisconsin State Board of Medical Examiners, 1915-1924; President, Board of Trustees, Northland College; former President of the Chicago and Northwestern and the Minneapolis, St. Paul and Sault St. Marie Railway Surgeons' Associations; former President of the Wisconsin State Medical Association; Councilor, Wisconsin State Medical Association, 1903-1930; Past President and one of the organizers of the Ashland Rotary Club; Thirty-second Degree Mason; Past Grand Commander, Knights Templar of Wisconsin; First Lieutenant in U. S. Army Medical Corps, World War I, advanced to Major in the Medical Reserve Corps, and made Chairman of the Medical Advisory Board; author, "The Autobiography of A Surgeon."

"His great product was professors."

Men of Medicine

A Gifted and Inspiring Teacher

About three years ago there was an auto accident, common enough in Los Angeles, in front of 397 Calaveras Street, Altadena. A woman from nearby Pasadena was injured, and a man wearing overalls and an old straw hat stopped cultivating his zinnias long enough to run out and see what he could do. She had a badly cut arm, so the gardening Good Samaritan made a tourniquet from a handkerchief to stop the bleeding, and then advised her to see her family doctor. A few days later a letter arrived addressed to the owner of the Calaveras Street house asking him to "thank your gardener for the prompt and intelligent help he gave me yesterday."

Dr. George Dock, physician and teacher of teachers, got a good chuckle out of being mistaken for a gardener. Today at 90, his penetrating blue eyes twinkling behind rimless spectacles, he recalls another period when he was often mistaken for someone else. That was when he was teaching at the University of Michigan in the 1890's. As was the universal custom in those days, he continued his own private practice and made many calls as a consultant; in wintertime he would accompany Ann Arbor doctors in their sleighs. He was in his thirties, and looked even younger. Many patients, therefore, thought he was the carriage boy, and that their family physicians were trying to pass him off as "the university professor" to impress them when the professor himself could not come.

Dr. Dock gained from his Michigan days a souvenir more lasting than memories. His fame has endured at the University and grown into legend. When Sinclair Lewis started to write "Arrowsmith" in 1923, 15 years after "Doc" Dock had left, he consulted another Michigan graduate, bacteriologist Paul de Kruif, for medical guidance. "Doc" Dock, according to Dock family tradition, served as the model for part of the composite character of "Dad" Silva, portrayed as the dean of the "Winnemac Medical School." In one memorable scene from the book, Silva-Dock (the late Dr. Victor C. Vaughan was dean at Michigan, so Dock represents the clinical half of the character) decided that the wife of a colleague did not have cancer of the stomach merely by taking her history and examining her abdomen. Then, to make sure he was right, he ordered her into the hospital for a test meal and x-ray.

The old-time doctors were like that. They could make accurate diagnoses without the aid of modern laboratory technics, because they had to. Dr. Dock started to practice medicine 10 years before the x-ray was discovered. In 1900, in a paper printed in the *Western Medical Review,* he advocated giving a patient a hot bath in order to relax the abdomen for a more accurate palpation. And in a paper given before the Nebraska State Medical Association in 1922 he reminded the doctors of the importance of inspection and palpation in detecting cancer of the stomach. For the expert and experienced old-timers, x-ray often served to confirm the diagnosis of which they felt reasonably sure after the first physical examination.

Dr. Dock, who retired three years ago from all practice and from formal teaching 28 years ago, is one of the most noted of the physician-teachers of the old school. He has been tough with his students, and patient with his patients, and stories about both aspects trail after him. While he was at the Washington University School of Medicine in St. Louis in 1920, the Red Cross appealed for doctors to fight a postwar typhus epidemic in the Balkans. Four of his residents and interns at the affiliated Barnes Hospital, where he was physician-in-chief, decided to volunteer, and went to ask him about it. Could he, they inquired, spare some or any of them? Dr. Dock asked which of them wanted to go, and was told that they all did. He growled: "Anytime I can't run the department without you, I ought to be fired." All of them went to the Balkans, and "Doc" Dock ran the department.

Another time, at Barnes Hospital, an intern was recounting the treatment he was giving a patient with a severe heart condition. "Doc" Dock wanted to know what drugs he was prescribing; two drops of tincture of digitalis, said the intern. Dr. Dock, trained by physicians who ladled out digitalis practically by the teaspoon, snorted: "Might as well try to spit out the Chicago fire."

But he was gentle with the patients he treated for so many years, and was impatient only with the well, never with the sick. He would often take ill medical students into his own home for better care. During the shortage of doctors in World War I, he never left his post at Barnes Hospital, even for weekends. He is tolerant of other people's foibles—as long as they are sick people's. One time

he made a sick call on a prominent woman temperance leader in St. Louis, and found at her bedside a bottle of the patent medicine Peruna; in those days it contained about 20 per cent alcohol. She had not expected him to notice, and was surprised into asking his opinion when he did; was it, she wanted to know, good for her? It was, he told her with a sly grin, "a good mild tipple."

"Doc" Dock could be tough with anybody endangering the welfare of his patients. In a paper given before the medical fraternity Nu Sigma Nu and reprinted in the *Journal of the American Medical Association* for January 31, 1920, he suggested a "counterstrike" by physicians against strikers, saying: "If a hospital cannot get coal or food, then no one in the unions concerned should be admitted to the care of such a hospital." But there is no record of his ever having turned any patient away, striker or not. He also had a deep concern over the question of how much a patient should know about the seriousness of his illness, and summed up his views in a paper given before the A.M.A. in 1904. He decided: "On the whole, in cases where the patients should know the truth the physician is often the best one to state it, and he should see that it is done before it is too late."

Dr. Dock carried some of his old-time German-school disciplinarian attitude over into his private life. For a time he was a great admirer of Theodore Roosevelt, the advocate of the "strenuous life." During vacations he would wear his hat turned up Teddy-style and adopted such Teddyisms as "Bully" and "Dee-lighted." But he outgrew that form of hero-worship. He has been, too, unsparing in criticism of the work of his two sons, whom he treats as students rather than patients. He comments with an urbane detachment both on the medical articles of his doctor-son, Dr. William Dock, professor of medicine at the New York State University Center at New York (formerly Long Island College of Medicine) and on the advertisements turned out by his older son, George Dock, Jr., New York copy writer.

Both his patience and his toughness stem from love of medicine. Dr. Dock told students of the graduating class of the University of Southern California's College of Medicine in 1905 that they must love their profession. He explained: "Unless you love your chosen career, no material return can raise it above the level of a trade, and a trade with many functions so repellant that they excite pity in the hearts of outsiders." "Doc" Dock loves his profession and his specialty, internal medicine. Some years ago he was summoned as a consultant to the bedside of the late Senator James Couzens, Henry Ford's onetime partner. A special train rushed him from St. Louis to Detroit, and the story got into the newspapers. Unfortunately, they referred to him as a "famous St. Louis surgeon." Later he fumed to his friend Surgeon Harvey Cushing: "If an internist gets into the papers it has to be as a surgeon!"

As a pioneer in scientific discoveries Dr. Dock twice missed the boat by medical minutes. When he was in Galveston as professor of pathology at Texas Medical College and Hospital, he suggested that the malaria parasite was transmitted by mosquitoes. This was in the late 1880's, more than 10 years before the cycle of man-mosquito-malaria was fully understood, and he might have been chronicled as the man to have made this discovery. He knew the parasite, all right, but he could not prove his suggestion because of a quirk of nature that was lucky for the people of Galveston, but unlucky for Dock. In Galveston, the only mosquitoes were not malaria-carriers. They were the Culex mosquito, like those in most of the U. S., not the malaria-carrying Anopheles genus.

Later, while Dock was at Michigan, a colleague, the noted Scottish pharmacologist Arthur Robertson Cushny, was first to recognize auricular fibrillation in dogs. He demonstrated the condition in dogs to his medical colleague, who tried in vain to prove that the same heart trouble caused the "delirium" of human patients, as Cushny suggested to him. With the development of the electrocardiograph about 10 years later, other researchers were able to prove that auricular fibrillation does exist in humans; it was the same disease discovered by Cushny in dogs. Dock had thought Cushny's guess was right, but neither got any credit for their work.

But while at Michigan—where he had a triple job as professor of pathology, medicine and psychiatry—Dr. Dock was the first to diagnose coronary thrombosis (as it is now called) in man during life. As Ralph H. Major writes in his *Classic Descriptions of Disease:* "While at the University of Michigan in 1896 he (Dock) published the first account of a case of coronary thrombosis in America diagnosed during life and confirmed by autopsy findings." The book includes an abstract of Dock's paper, "Notes on the Coronary Arteries," and an account of the history-making patient, a Mr. B., a 64-year-old lumber dealer. Dr. Dock concluded: "In this case the relation of the coronary sclerosis to the gradually developing dyspnea, and of the infarction to the acute attack, is clear."

While still at Michigan he and his colleagues, in 1907, made the then startling assertion that leukemia and Hodgkin's disease were not due to infections, but were tumors. They were so far out ahead that their contemporaries thought they were just plain silly; since fever accompanied the diseases, the scoffers reasoned, infection just had to be the cause. Standard textbooks 30 years later still made the positive assertion that Hodgkin's disease is infectious. There is still some argument about

Hodgkin's disease, but leukemia is now generally recognized as neoplastic in origin.

Dr. Dock also did a pioneering job in alerting the U. S. to the danger of hookworm as a gnawing blight in the South. The book, *Hookworm Disease: Etiology, Pathology, Diagnosis, Prophylaxis,* written with Dr. Charles C. Bass, first published in 1910, did much to puncture American complacency about the disease. Hookworm had been known in Europe, but this country was thought to be free of it because of our higher standards of living and sanitation. The book stirred up a lot of excitement, and did much to start an all-out drive to eradicate the disease. His studies of anemia led to better diagnosis, but produced no great advance in treatment.

But "Doc" Dock's greatest work was in the training of other doctors; his great product was professors. As Major's book points out: "Dock is a gifted and inspiring teacher and has left his impress upon all his students and upon the medical schools with which he has been associated." He had a large part in building the great Washington University School of Medicine in St. Louis. When he went there in 1910 it was a small school, located in downtown St. Louis. As dean and influential professor of medicine he was the school's stimulant and excitant for 12 years. He helped assemble a fulltime faculty, and he himself was one of the first fulltime professors of medicine in the United States, giving up all private practice. An old-timer but no conservative, he was one of the first medical school professors to become a "man in white" on hospital rounds, as he switched from the traditional Prince Albert coat and striped trousers to a simple white canvas coat.

The group of teachers he helped to bring together made history. Members of the faculty of Washington University have won more Nobel prizes than those of all other U. S. medical schools combined. While at St. Louis "Doc" Dock trained men who were to hold chairs as professors of medicine at seven U. S. medical schools, while several of his former students, like their mentor, became builders of medical schools.

There were many doctors in the Dock family, all of them known, of course, as "Doc" Dock. A great uncle was a doctor, as was an uncle; there was also a non-Dock doctor on his mother's side of the family. The Docks are collateral descendants of Pennsylvania's famed eighteenth century "Skippack schoolmaster" Christopher Dock, but there is no record he was called "Doc." Dr. William Dock's two sons have shown no inclination for medicine, but his nephew is starting on a medical career this year.

George Dock was born in the small coal-mining town of Hopewell, Pennsylvania, on April 1, 1860, the son of a mining engineer, Gilliard Dock, and the former Lavinia Lloyd Bombaugh. A sister, also named Lavinia, well known as a pioneer nurse, historian of nursing and as a militant suffragette, still lives in Pennsylvania. He attended the Harrisburg (Pa.) Academy, a boys' school, where he was serious, quiet and friendly. He was early interested in natural science and made an herbarium of specimens collected in the region of Harrisburg. He was fascinated by the idea of evolution, then much discussed, and by 13 he could toss around words like protoplasm. One day at dinner one of his five sisters asked him what his eventual career would be, and he answered casually: "What do you think of medicine?"

Firmly convinced that he had found the answer, young Dock went to the University of Pennsylvania and received his M.D. in 1884; the university was to give him the honorary degree of Sc.D. twenty years later. From 1887 to 1888 he was assistant in clinical pathology at the university under Sir William Osler. Osler was to write later of his days in Philadelphia: "There was no clinical laboratory, only an improvised room under the amphitheater, which was very active the year George Dock was in charge," and he called him "a man who knows more about clinical laboratory procedures than anyone in the U. S." Dr. Dock never lost interest in pathology; clinical microscopy, which proves tiresome to many physicians, has always fascinated him.

In 1889 he went to Texas Medical College and Hospital as professor of pathology and clinical medicine, speculated about mosquitoes and malaria, and went on to Michigan—then the best medical school west of Philadelphia—in 1891, and stayed until 1908. While at Michigan, he married, in 1892, Laura McLemore.

The dean of medicine at Michigan, Dr. Vaughan, wrote later in his book, *A Doctor's Memories:* "From 1891 to 1908 George Dock served as professor of the theory and practice of medicine, and I am sure that in this capacity he had but few equals and no superiors. He lived in the laboratory and in the wards of the hospital. His original contributions to scientific medicine won recognition throughout the world. As a teacher he initiated his students in scientific investigations and demonstrated the value of research work in the treatment of disease."

The Spanish-American War provided an exciting sabbatical while he was at Michigan. He served as acting assistant surgeon of the Army, and spent the war fighting a campaign of his own. In many Army camps in the U. S., there was an epidemic of typhoid, but the Army authorities would not admit it, nor would they allow autopsies, fearing unfavorable reaction from the public. Instead,

they insisted that the men were dying of malaria or the nonexistent disease "typhomalaria." Dr. Dock made investigations at Chickamauga, Knoxville and Meade. He and other Army surgeons kept fighting for the right to perform autopsies to prove whether or not the epidemic was typhoid. In the summer of 1898 the government finally appointed a typhoid commission, headed by Walter Reed; other members were Major Edward O. Shakespeare and Dr. Vaughan. The commission was able to prove that typhoid was to blame, and to force sanitation measures to cope with it.

Dr. Dock was still outraged by the official obstinacy six years later, and wrote a paper that was one of the most eloquent paeans to pathology ever written. He said: "In the lavish waste of life and health that occurred in Army camps in the Spanish-American War it was no less instructive than depressing to see the neglect of pathologic anatomy. For weeks the question as to whether there was typhoid fever in the camps was met by contradictory assertions. It took months to get microscopes, cultures and capable observers to the hospitals. Yet a half-dozen autopsies could have settled the problem very quickly. While large sums were spent for instruments to treat wounds that never came, some of the largest hospitals did not possess a single autopsy instrument. It was said by those in high places that people would not like to have the dead soldiers examined; but can we suppose that those who were willing to let their sons risk the mutilation of the machete would object to a decent autopsy if they realized its value, or that men who thought it was sweet and glorious to die for their country would not be willing to be examined post mortem for the benefit of others?"

Dr. Dock has always been a tough and vigorous fighter in medical campaigns, many of them long since won. He fought for vaccination against smallpox at a time when it was under attack by organized "antivaccinationists." Aroused by the prevalence of goiter in Michigan, he challenged medicine to solve the problem of goiter. He fought against irregular practitioners, such as chiropractors, whom he considered dangerous. In the A.M.A. *Journal* for January 7, 1922, he gave an amusing account of a visit to a chiropractic school, where, he said with quiet understatement, he had gone "without announcing myself."

In 1908 Dr. Dock became professor of the theory and practice of medicine at Tulane University, where his interest in hookworm started. While there he wrote one of his most witty and often-quoted papers, "Spelling as an Index to the Preparation of the Medical Student." He cited as the appalling spelling errors of a student with an A.B. degree "afasia," "paracite," "irruption" for "eruption." Other horrors he recorded in a now-familiar complaint about lack of academic training of medical students were "bowals" for "bowels," and "dissease" for "disease"; most of them could spell "physician." He raged at would-be physicians who could write "pulse are rapid," "a sequelae of," "gastritis of the stomach," "a protozoa" and "plumb colored." Said he wrathfully: "Physicians who should make such blunders will be made to feel ashamed, or will be looked on with condescension by educated men and women." He also could give slily humorous titles to his own papers, such as "The Advantage of Using Potassium Iodide Until We Have Something Better," delivered at the A.M.A.'s 1909 meeting at Atlantic City.

Dr. Dock left Tulane for Washington University in 1910, to reach there the peak of his career. In order to make generally available Dr. Dock's method of running Barnes Hospital, Dr. George R. Herrmann wrote "Methods in Medicine: the Manual of the Medical Service of Dr. George Dock," first published in 1924. The book explains in detail the duties of the hospital staff, from chief residents to clinical clerks. It gives the recipe for the "Dock test breakfast," which consists of 30 gm. of dry shredded wheat biscuit, to be chewed by the patient with the anemic help of 400 cc. of water. It also carries the famous list of "Dock's Twenty Drugs." He had begun to lecture on the renowned twenty at Michigan because, he explained, "proficiency in the use of a few drugs was infinitely more valuable to the student and practitioner than a smattering of every item in the old Materia Medica." His lectures were in fact an antidote to the over-drugging of the times. Many of these drugs, such as quinine, digitalis, strychnine, etc., are still in use, but courses in the "twenty drugs" are given no longer.

In 1922, three years before he was due to retire, Dr. Dock resigned from the Washington University Medical School. He felt he had been professor of medicine "too long"—34 years—and that it was time to give younger men a chance. Cushing later chose to retire at the same age, 62. Two other factors influenced his decision. The faculty had voted to increase the number of students by about 50 per cent; Dock disagreed because he thought there were not enough clinical facilities to give the enlarged student body proper training. And for many years he had been a victim of sinus infection, a serious condition in those days of vigorous therapy and radical surgery.

So "Doc" Dock decided to move to California and return to the private practice of medicine he had abandoned 12 years before. He had written, in 1906, a kind of guide book for young doctors moving into a new community. In an address to the graduating class of the University of Michigan on "Medical Ethics and Etiquette" he had given advice on such practical matters as professional signs, telling the graduates they should "not have

Medical history is a hobby of Dr. Dock, who has contributed much to the making of that history.

a big sign in a town where it is the proper thing to have a small one." In private conversation he is fond of illustrating the point by telling the story of a doctor who moved into a New England town and put up a sign announcing that he was a "specialist in circumcision." His colleagues chided him, and suggested he look around the town to see what New Englanders did. So he amended his sign to read "Ye Olde Yankee Clipper."

"Doc" Dock had a medicine bag full of stories, especially regional ones, to draw on when he went around lecturing. If some chauvinistic chairman, for instance, would brag of California, he would reply, "Ah, yes, the land of the lemon, the prune and the nut." Or he would describe Texas as the state where "there are more rivers and less water, more cows and less milk, where you see farther and see less than anywhere else in the world."

In Los Angeles, Dr. Dock practiced internal medicine, mostly as a consultant. Many of his patients were retired school teachers, retired doctors and their wives, and old friends, so his income was never large. During the depression of the thirties he complained humorously: "I can't make out whether there is a falling off of morbidity or of curiosity among the plutocrats." He continued to lecture and write, adding to the total of well over 100 published papers on medicine and medical history. One of his last important papers was the Frank Billings lecture, "Historical Notes on Coronary Occlusion," delivered before the A.M.A. at its 1939 meeting in St. Louis. He helped develop the Los Angeles County Medical Society's library, and gave it some of the medical texts he had collected through the years. In appreciation, the society established the George Dock Lectureship in the History of Medicine—one of his chief interests—in 1940; Dr. Dock himself was the first lecturer. In 1944 he was given the Distinguished Service Medal and Award of the A.M.A. His first

wife died while he was in California, and in 1925 he married again, the former Miriam Gould.

"Doc" Dock has always been a tough and vigorous vacationer as well as campaigner, and on outings he has spared himself as little as he has spared his students. He has made many pack trips in Alaska, Arizona, Wyoming and the National Parks. He started visiting the north rim of the Grand Canyon when it was a five-day trip by a four-horse wagon from the railhead. At 59 he climbed to the top of Mt. Whitney in California, the highest mountain in continental U. S. At 60, he made a pack trip to Rainbow Bridge in Utah. The party ran out of food, and they had to ride from 6:30 A.M. to 10:30 P M. to reach a waterhole. At the end of the trip the guide and cook were fagged out; "Doc" Dock was feeling fine. At 77, in 1937, just back from a trip around the world, he made an 18-mile horseback tour along the Grand Canyon, from Bright Angel Point. In 1910, when he was 60, he had a narrow escape from death along the north rim of the Grand Canyon at a point then called Molly's Nipple, now known by a politer name. He was taking photographs when he slipped and slid down the canyon wall until his clothes caught on a cedar tree and he was violently yanked to a stop. He escaped with a diaphragmatic hernia, of which he was not aware until years later.

He has long been interested in photography, and experimented with early color processes in both still and movie films. Like many other doctors, he has been fond of photographing landscapes, and he has made some notable ones of the Grand Canyon and of Rainbow Bridge. In St. Louis, after returning from one of his trips, he would give a party and lure his friends into coming to look at his lantern slides. Some would fall asleep. He never could understand his friends' lack of enthusiasm for his shows. But in later years he came to realize how boring others' travel talks could be, as relatives and friends often made him the guest of honor at such exhibits.

Fond of travel, he made many trips abroad. He was vice president of the International Medical Congress that met in Moscow in 1897, Budapest in 1909 and London in 1913. He knew the leading doctors of Germany, France and England. He would drop in on them, spend a few days in Munich or at the Pasteur Institute in Paris, and return with the latest in European medical developments to use in his own teaching and doctoring.

In California, he has lectured occasionally at the University of Southern California, where he has been honorary professor of medicine since 1932. Little interested in medical politics, he has held few offices. He is a member of the A.M.A., the California State Medical Association, the Los Angeles County Medical Society, the Association of American Physicians (president 1916-1917), the New York Academy of Medicine, the American Society of Tropical Medicine, the American Association of Medical History. He is a fellow of the American Association for the Advancement of Science. In addition to his degrees from the University of Pennsylvania, he holds an honorary degree of A.M. from Harvard (1895) and of LL.D. from the University of Southern California (1936). He has had little time for such social activities as bridge, but enjoyed an occasional evening of Liedersinging. He belongs to the University and Valley Hunt Clubs in Pasadena and the Athletic Club in Los Angeles.

THREE years ago Dr. Dock retired after 25 years of practice in the Los Angeles area, as he had begun to "enjoy poor health" occasionally. He was unable to attend last spring's George Dock lecture. He has given up his hobby of photography, but still works with his flowers. He continues writing his memoirs, which he began several years ago. He reads less medical literature now, but enjoys current magazines and an occasional novel or biography. He continues to work with the Los Angeles County Medical Society Library. Hanging on the wall of his study, over his old-fashioned golden-oak desk, is a beautifully printed poem in French, the work of the sixteenth century French printer Plantin. The poem's last line advises men "to cultivate your little place and wait peacefully for death."

GEORGE R. BURNS

The Medical Bookman

PEPTIC ULCER*

THREE forewords introduce this extraordinary volume. Sara M. Jordan says: "This momentous book may well be labelled the magnum opus of a man who has always been a stimulating example of undaunted courage and energy in attacking a problem, for in it the problem of peptic ulcer has been attacked, analyzed, and set before us in all its phases in an unprecedented form." Dr. Donald C. Balfour writes: "A milestone in the history of peptic ulcer." Dr. A. J. Carlson adds: "This is a *must* book, not only for our colleagues in general practice but also for our colleagues in internal medicine, surgery, psychiatry and physiology."

The book which merits these encomiums has required some fifteen years for its preparation. Over 5,000 contributions to medical literature have been consulted. The important factors essential for the formation of peptic ulcer are set forth. The diagnosis and medical and surgical treatments are fully elucidated. Each chapter has a summary and each section has a summarizing chapter. The photographs and drawings were prepared especially for this book. The bibliographic references have been checked repeatedly and the index of authors is a model.

"A peptic ulcer is a benign, nonspecific ulcer located in those portions of the alimentary tract bathed by gastric juice." The chapter on physiology hardly wastes a word in its succinct description of the motor activities and secretions of the stomach. Ulcers are exceedingly rare in animals and for experimentation must be artificially produced. The chapter proving that the stomach, intestines and pancreas fail to digest themselves for reasons intimately related to the appearance of ulcer is a guide to prevention of ulcer through study of the mechanisms of secretion and of pathologic change. The investigations of healing indicate that chronic peptic ulcer possesses almost normal potentialities for healing when placed under favorable conditions—for example strict medical management. Acid contributes to a delay in healing; the same is true, the authors point out, of gastric retention, and mechanical trauma due to rough food, particularly in the case of the stomach.

Almost 600 pages are devoted to the pathogenesis of peptic ulcer. Here is the brief summary:

> Acute gastric or duodenal ulcer arises from (a) mechanical or chemical trauma, or (b) a vascular disturbance secondary to some toxic substance, as in burns, or (c) a vasoneurotic, infectious, or allergic mechanism, as in an aphthous ulcer of the buccal mucosa. The acute lesion extends or is kept from healing by (a) acid-pepsin in normal or hypernormal amounts, or (b) mechanical and chemical trauma from rough and irritating food, or (c) hypermotility or hypertonicity of the musculature. In some populations, a dietary deficiency is probably concerned. In some cases, secretion of excessive amounts of acid causes the initial lesion and prevents it from healing. In many cases, excessive secretion of acid does not occur and hence some deficiency in the mucosa must be concerned. In any case a bland, nonmechanically irritating diet which buffers and neutralizes acid should promote healing of the ulcer.

The paragraph just cited bears reading and rereading and perhaps even memorizing because it is the rationalization of all successful medical methods of treating ulcer thus far known and reasonably well established.

The section on diagnosis is complete, direct and wholly adequate. Then come the sections on medical and radiologic therapy and that on surgical therapy.

Chapter 24, the final chapter in this wonderful contribution to the literature of peptic ulcer is a "Summary of Therapy." The statements are all significant; their flavor is apparent in the following quotations:

> "A complete Sippy management prevents recurrences better than other medical regimens."
>
> "It is generally agreed, though further evidence is required, that approximately 80 per cent of ulcer patients respond satisfactorily to medical management over a period of years."
>
> "A schedule of frequent feedings with or without an antacid and with or without hospitalization will provide relief from distress within two or three days in at least 85 per cent of patients."

*By A. C. Ivy, M.D., Chairman of the Department of Clinical Sciences, University of Illinois; M. I. Grossman, M.D., Associate Professor of Physiology; and William H. Bachrach, M.D., Research Associate in Physiology, University of Southern California School of Medicine. 1,144 pages with 137 illustrations. 1950, The Blakiston Company, Philadelphia. $14.00.

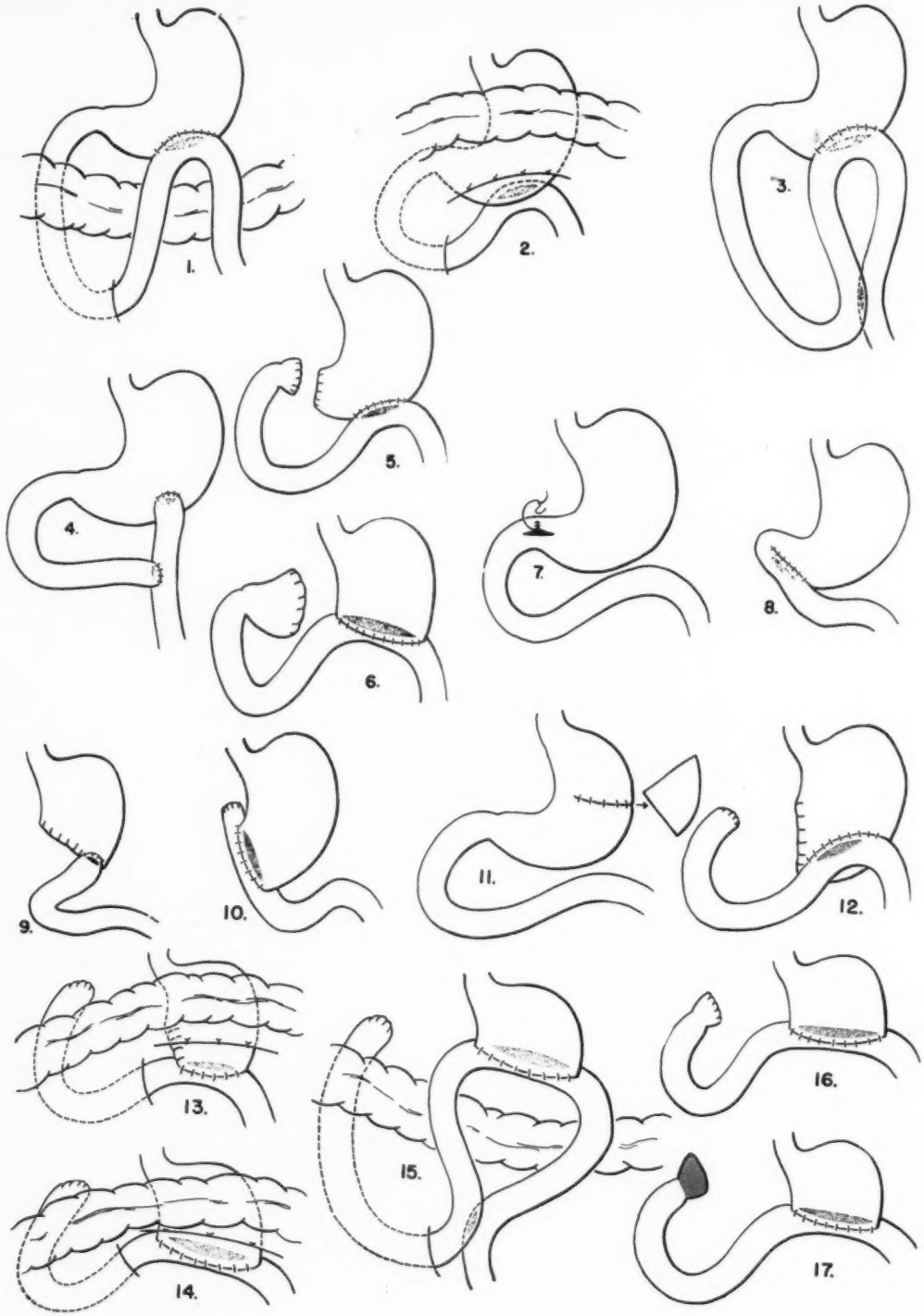
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FIGURE 134. Various operations which have been used for the treatment of peptic ulcer:

1. Anterior gastrojejunostomy (gastroenterostomy).
2. Posterior gastrojejunostomy (gastroenterostomy).
3. Gastroenterostomy with (Braun's) enteroenterostomy.
4. Gastroenterostomy with Roux-en-Y anastomosis.
5. Gastroenterostomy with pyloric exclusion (von Eiselsberg).
6. Devine's pyloric exclusion operation (no stomach is resected).
7. Heineke-Mikulicz pyloroplasty.
8. Finney pyloroplasty (gastroduodenostomy).
9. Billroth I gastric resection.
10. Finney-Haberer modification of Billroth I gastric resection.
11. Connell's fundusectomy.
12. Billroth II gastric resection.
13. Hofmeister modification of Billroth II gastric resection (posterior or retrocolic anastomosis).
14. Pólya modification of Billroth II gastric resection (posterior or retrocolic anastomosis).
15. Pólya type gastric resection with anterior (antecolic) anastomosis and enteroenterostomy.
16. Finsterer's resection with pyloric exclusion (the remnant of the pars pylorica is not resected).
17. Finsterer's resection with pyloric exclusion and excision of the pyloric mucosa (the mucous membrane of the excluded pyloric remnant is excised).

(From: "Peptic Ulcer" by Ivy, Grossman and Bachrach.)

"Acute perforated peptic ulcer is generally considered to be a direct and immediate indication for operation."

"Vagotomy alone in the hands of the average experienced surgeon appears to yield no better results than simple gastroenterostomy, since the incidence of recurrences and unsatisfactory results is approximately the same."

"A comparison of the results of the medical and surgical management of those ulcer patients who have been hospitalized indicates that surgery promises fewer recurrences and a greater chance of becoming continuously symptom-free. However, the mortality of medical management is lower than that of surgical management."

This book is well printed on good stock; the typographical errors are few indeed. The illustrations by their quality and educational value, the indexes by their completeness and accuracy, and the literary style of the writing make this what Dr. Sara Jordan called it, "a magnum opus."

M. F.

► YEAR BOOK OF PHYSICAL MEDICINE AND REHABILITATION - - -

Edited by Frank H. Krusen, M.D., Professor of Physical Medicine, Mayo Foundation; Head of the Section on Physical Medicine, Mayo Clinic, and Howard A. Rusk, M.D., Professor of Physical Medicine and Rehabilitation, New York University College of Medicine; Chairman of the Department of Physical Medicine and Rehabilitation, Bellevue Hospital, New York City. Associate Editors: Earl C. Elkins, M.D., Winifred Overholser, M.D., and George G. Deaver, M.D. 456 pages, with 131 figures. 1950, Year Book Publishers, Inc., Chicago. $5.00.

Edited primarily to present a comprehensive review of the most recent literature in the fields of physical medicine and rehabilitation, this compilation of facts results from an extensive perusal of the related publications advanced during the past year. This volume is divided into three main topics, and offers for the first time a section on occupational therapy which has only recently been associated with the field of physical medicine.

It is noteworthy that the remaining subdivisions of physical medicine and rehabilitation are no longer mainly concerned with the clinical application of the technics of Physical Medicine, but are directing their efforts towards clinical and physiologic research. Today's contemporary literature reflects this tendency with a remarkable increase in the number of published articles concerned with research and basic interpretation. Great strides have been made in Physical Medicine especially in laboratory and clinical research, because of the

demand for adequate treatment of war injuries in addition to the stimulation of the various committees and foundations interested in its development. Furthermore, the increased number of physicians in the field and the establishment of training programs at university centers help to direct the research into proper channels.

While certain specialties such as orthopedics and geriatrics are mainly benefited by the advances in physical medicine, it is readily recognized that all branches of medicine and surgery have patients who would be helped by physical therapy.

H. O'P.

► PROCTOLOGY IN GENERAL PRACTICE - - -

By J. Peerman Nesselrod, B.S., M.S., M.Sc. (Med.), M.D., F.A.C.S., F.A.P.S., Associate in Surgery, Northwestern University Medical School; Associate of Surgical Division of Proctology, Evanston Hospital, Evanston, Ill. 276 pages, with 64 figures. 1950, W. B. Saunders Company, Philadelphia & London. $6.00.

This book contains a very complete and concise explanation of proctologic problems in general, primarily presented for general practitioners, medical students, and house officers. The material is covered in fifteen chapters and includes all the anorectal problems with which one would be confronted. There is considerable emphasis on anatomy and physiology which gives one a fundamental working basis for a clearer understanding of anorectal problems.

The ordinary diagnostic procedures are described in detail and the proctologic examinations in relation to other fields of medicine should be a great aid to the general practitioner and the general surgeon in their daily work.

It is the author's opinion that the surgical management of common anorectal inflammatory diseases is based upon the concept of anal infection as the chief etiologic agent. Nesselrod emphasizes the importance of postoperative care in order to attain the ultimate goal in anorectal surgery—that of a satisfactory functional result. The accomplishment of this goal requires close cooperation of patient and surgeon. He further states that proctoscopy constitutes the most important diagnostic method in the early diagnosis of and the study of rectal and colonic cancer. Further, he is enthusiastic in encouraging the widespread use of the proctoscope in routine physical examinations of the terminal bowel.

R. J. T.

Books received will be acknowledged in this department each month. As space permits, books of principal interest to our readers will be reviewed more extensively.

The Antihistamines; Their Clinical Application. By Samuel M. Feinberg, M.D., Associate Professor of Medicine, Chief of Division of Allergy and Director of Allergy Research Laboratory; Saul Malkiel, Ph.D., M.D., Assistant Professor of Medicine, Director of Research, Allergy Research Laboratory; and Alan R. Feinberg, M.D., Clinical Assistant in Medicine, Attending Physician in Allergy Clinic, Northwestern University Medical School. 291 pages. 1950, The Year Book Publishers, Inc., Chicago. $4.00.

Cerebral Palsy. By John F. Pohl, M.D., Orthopedic Surgeon, Michael Dowling School for Crippled Children, Minneapolis, Minnesota. 224 pages, with 131 illustrations. 1950, Bruce Publishing Company, St. Paul, Minnesota. $5.00.

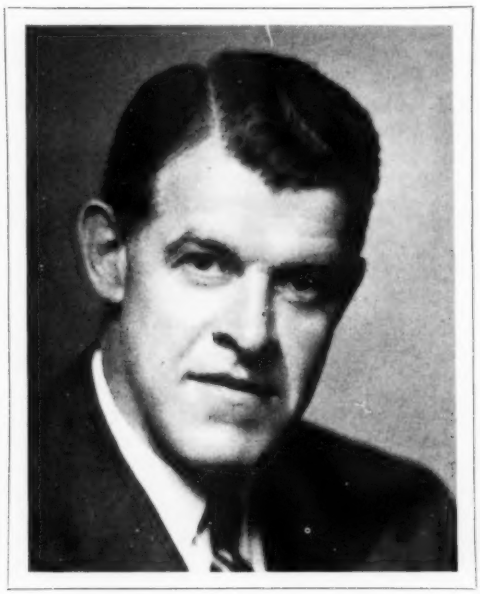
The Meaning and Practice of Psychotherapy. By V. E. Fisher, Ph.D., Psychologist and Psychotherapist, Formerly Assistant Psychologist, Worcester State Hospital; Assistant Professor of Psychology and Director of the Mental Clinic, New York University, Washington Square College; Psychologist and Psychotherapist, Idaho State Hospital South. 411 pages. 1950, The Macmillan Company, New York. $5.00.

A Textbook of Venereal Diseases. By R. R. Willcox, Consultant in Venereal Diseases, St. Mary's Hospital, London; Physician-in-Charge, Venereal Diseases Department, King Edward VII Hospital, Windsor. 439 pages, with 154 figures. 1950, Grune & Stratton, Inc., New York. $5.00.

Cerebral Palsy Equipment. Prepared and published by the National Society for Crippled Children and Adults, Inc., sponsored by Zeta Tau Alpha, National Fraternity for Women 268 pages, illustrated. $3.75.

Association Notes

THIRTY-FIFTH ANNUAL ASSEMBLY OFFERS COMPREHENSIVE PROGRAM



RICHARD B. CATTELL

WALTMAN WALTERS

PHYSICIANS who attend the 35th Annual International Assembly of the Interstate Postgraduate Medical Association at the Hotel Stevens in Chicago, November 6 through 9, will have the opportunity of hearing 56 leading authorities in their respective fields in an unparalleled program of clinics and addresses.

Conducted on a rigid time schedule which permits each speaker exactly one-half hour, this unique Assembly is devoted exclusively to the continuing education of practicing physicians and continues its 35-year policy of offering the latest and most authoritative information from every field of medicine and surgery.

In addition to the four-day comprehensive scientific program, there will be a large and attractive display of technical exhibits showing the newest proved pharmaceutical products, instruments, equipments and publications. One-hour intermissions are scheduled each morning and afternoon to provide ample time for viewing these exhibits and talking with the exhibitors. All lectures and clinics, as well as the technical exhibit, will be in the spacious Hotel Stevens.

Chairman of the Chicago committee on arrangemens is Dr. Warren H. Cole, professor of surgery at the University of Illinois College of Medicine and president of the Chicago Medical Society. Members of the Clinic committee are: Chairman, Dr. LeRoy H. Sloan, and Drs. Wright Adams, John A. Bigler, Frederick H. Falls, Philip Lewin, Walter G. Maddock, Karl A. Meyer, Willis J. Potts, and Willard O. Thompson.

Dr. Richard B. Cattell of the Lahey Clinic, Boston, 1950 president-elect of the Association will assume office at the Assembly Dinner to be held in the Grand Ballroom of the Hotel Stevens on Wednesday evening, November 8. Dr. Cattell will succeed Dr. Waltman Walters, Mayo Clinic and professor of surgery, Mayo Foundation, University of Minnesota Medical School, Rochester.

Full details of the scientific program, the technical exhibit and the Assembly dinner will be found on pages 336 to 341 of this issue.

Chicago Assembly Program

INTERSTATE POSTGRADUATE MEDICAL ASSOCIATION

Hotel Stevens — Chicago — November 6–9, 1950

Monday, November 6

8:00 A.M.

8:00 Diagnostic Clinic: "The Medical Aspects of Hypertension."

Dr. Wright Adams, Professor and Chairman of the Department of Medicine, University of Chicago School of Medicine, Chicago, Illinois.

8:30 Diagnostic Clinic: "Hemicolectomy in The Treatment of Carcinoma of The Left Colon."

Dr. Karl A. Meyer, Professor of Surgery, Northwestern University Medical School; Medical Superintendent, Cook County Hospital, Chicago, Illinois.

9:00 Diagnostic Clinic: "The Relationship of Chronic Cystic Mastitis to Cancer of The Breast."

Dr. Harry A. Oberhelman, Professor and Chairman of The Department of Surgery, Loyola University and Stritch School of Medicine, Chicago, Illinois.

9:30 Diagnostic Clinic: "Bronchial Asthma in The Farm Population."

Dr. Leon Unger, Associate Professor of Medicine, Northwestern University Medical School; Attending Physician at Cook County Hospital and at Wesley Memorial Hospital, Chicago, Illinois.

10:00-11:00 *Intermission for Review of Exhibits*

11:00 Diagnostic Clinic: "Disorders of The Adrenal Cortex in The Light of Recent Observations with ACTH and Cortisone."

Dr. Willard O. Thompson, Clinical Professor of Medicine, University of Illinois College of Medicine; Past-President, Chicago Medical Society, Chicago, Illinois.

11:30 Diagnostic Clinic: "The Management and Outlook of Coronary Disease."

Dr. Robert S. Berghoff, Clinical Professor of Medicine, Loyola University and Stritch School of Medicine; Senior Attending Physician and Senior Cardiologist, Mercy Hospital-Loyola University Clinics; Member, Board of Education, City of Chicago, Chicago, Illinois.

Noon Intermission

1:30 P.M.

1:30 Diagnostic Clinic: "Disturbances of Cerebral and Coronary Circulation Caused by Chronic Pulmonary Disease."

Dr. William S. McCann, Charles A. Dewey Professor of Medicine, University of Rochester School of Medicine; Physician-in-Chief, Strong Memorial Hospital, Rochester, New York.

2:00 Address: "Selection of Cases and Practical Points on The Administration of ACTH."

2:30 Address: "Brain Tumors: A Study of Postoperative Results and Survival Periods."

Dr. Alfred W. Adson, Section on Neurological Surgery, Mayo Clinic; Professor of Neurosurgery, University of Minnesota Graduate School of Medicine, Rochester, Minnesota.

3:00-4:00 *Intermission for Review of Exhibits*

4:00 Address: "The Use and Abuse of The Dextrose Tolerance Test."

Dr. Samuel Soskin, Professorial Lecturer in Physiology, University of Chicago School of Medicine; Director, Medical Research Institute, Michael Reese Hospital; Dean, Michael Reese Hospital Postgraduate School, Chicago, Illinois.

4:30 Address: "Highlights in Medical Ophthalmology with Special Reference to Glaucoma." (The Schneider Foundation Eye Presentation.)

Dr. Conrad Berens, Professor of Clinical Ophthalmology, New York University-Bellevue Medical Center, Postgraduate Medical School, New York, New York.

5:00 Address: "Intracranial Aneurysms."

Dr. James L. Poppen, Neurological Surgeon, Lahey Clinic, New England Deaconess, Boston Psychopathic and New England Baptist Hospitals, Boston, Massachusetts.

Dinner Intermission

7:30 P.M.

7:30 Address: "The Treatment of Ruptured Peptic Ulcer."

Dr. Sam F. Seeley, Brig. Gen., Medical Corps, Chief of Surgical Service, Walter Reed General Hospital, Washington, D. C.

8:00 Address: "Value of Routine Anal-Rectal Examinations in General Practice."

Dr. Malcolm R. Hill, Professor of Proctology, College of Medical Evangelists School of Medicine; Attending Proctologist, California, Los Angeles County and White Memorial Hospitals; Proctologist, Southern Pacific Railroad Company, Los Angeles, California.

8:30 Address: "Evaluation of Antibiotic Therapy."

Dr. Chester S. Keefer, Wade Professor of Medicine, Boston University School of Medicine; Director, Robert Dawson Evans Memorial Hospital; Physician-in-Chief, Massachusetts Memorial Hospital, Boston, Massachusetts.

9:00 Address: "Primary Hyperparathyroidism."

Dr. Llewelyn P. Howell, Clinical Section, Mayo Clinic, Rochester, Minnesota.

Tuesday, November 7

8:00 A.M.

8:00 Diagnostic Clinic: "Cryptogenic Fever."

Dr. LeRoy H. Sloan, Clinical Professor of Medicine, University of Illinois College of Medicine, Chicago, Illinois.

8:30 Diagnostic Clinic: "Atresia of The Esophagus with or without Tracheo-Esophageal Fistula."

Dr. Willis J. Potts, Professor of Surgery, Northwestern University Medical School; Surgeon-in-Chief, Children's Memorial Hospital, Chicago, Illinois.

9:00 Diagnostic Clinic: "Carcinoma of The Colon."

Dr. Warren H. Cole, Professor of Surgery, University of Illinois College of Medicine; President, Chicago Medical Society; General Chairman, Interstate Postgraduate Medical Association Chicago Committee, Chicago, Illinois.

9:30 Diagnostic Clinic: "Non-Allergic Asthma."

Dr. Harry L. Alexander, Professor of Clinical Medicine, Washington University School of Medicine, St. Louis, Missouri.

10:00-11:00 *Intermission for Review of Exhibits*

11:00 Diagnostic Clinic: "Thyroid Disease Today in The Light of Newer Developments."

Dr. Frank H. Lahey, Director, Lahey Clinic; Surgeon, New England Deaconess Hospital; Surgeon-in-Chief, New England Baptist Hospital, Boston, Massachusetts.

11:30 Diagnostic Clinic: "Backaches and The Disk Syndromes."

Dr. Philip Lewin, Professor of Bone and Joint Surgery, Northwestern University Medical School, Chicago, Illinois.

Noon Intermission

1:30 P.M.

1:30 Diagnostic Clinic: "Thrombo-Embolism: Its Cause and Prevention."

Dr. Alton Ochsner, William Henderson Professor of Surgery and Director of the Department, Tulane University of Louisiana School of Medicine; Director of Section on General Surgery, Ochsner Clinic, New Orleans, Louisiana.

2:00 Diagnostic Clinic: "The Diagnosis and Treatment of Ileitis."

Dr. Charles W. Mayo, Surgical Section, Mayo Clinic; Professor of Surgery, University of Minnesota Graduate School of Medicine, Rochester, Minn.

2:30 Address: "The Diagnosis of Malignant Ovarian Tumors."

Dr. Frederick H. Falls, Professor of Obstetrics and Gynecology and Head of the Department, University of Illinois College of Medicine, Chicago, Illinois.

3:00-4:00 *Intermission for Review of Exhibits*

4:00 Address: "Management of Occiput Posterior."

Dr. John L. McKelvey, Professor of Obstetrics and Gynecology and Head of the Department of Obstetrics and Gynecology, University of Minnesota Medical School, Minneapolis, Minnesota.

4:30 Address: "Some Practical Pointers About Cross-Eyes."

Dr. Emanuel Krimsky, Adjunct Professor of Ophthalmology, New York Polyclinic Medical School, Brooklyn, New York.

5:00 Address: "Developmental Diagnosis."

Dr. Arnold Gesell, Director Emeritus, Clinic of Child Development; Professor Emeritus of Child Hygiene; Research Associate in Vision Research, Yale University School of Medicine; Gesell Institute of Child Development, New Haven, Conn.

Dinner Intermission

7:30 P.M.

7:30 Address: "Sludged Blood."

Dr. Melvin H. Knisely, Chairman of The Department of Anatomy, Medical College of the State of South Carolina, Charleston, South Carolina.

8:00 Address: "The Problem of The Bleeding Nipple."

Dr. John W. Cline, Associate Clinical Professor of Surgery, Stanford University School of Medicine, San Francisco, California; President-Elect, American Medical Association.

8:30 Address: "Therapeutic Indications for Vitamins in Mixtures."

Dr. Tom D. Spies, Professor and Head of the Department of Nutrition and Metabolism, Northwestern University Medical School, Chicago, Illinois; Director, Nutrition Clinic, Hillman Hospital, Birmingham, Alabama.

9:00 Address: "The Mask of Sanity."

Dr. Hervey M. Cleckley, Professor of Psychiatry and Neurology, University of Georgia School of Medicine, Augusta, Georgia.

Wednesday, November 8

8:00 A.M.

8:00 Diagnostic Clinic: "Causes of Failure in The Surgical Treatment of Hypertension."

Dr. Geza de Takats, Clinical Associate Professor of Surgery, University of Illinois College of Medicine, Chicago, Illinois.

8:30 Diagnostic Clinic: "Pathologic Physiology of Mitral Stenosis."

Dr. Richard V. Ebert, Clinical Associate Professor of Medicine, University of Minnesota Medical School; Chief of Medical Service, Veterans Administration Hospital, Minneapolis, Minnesota.

9:00 Diagnostic Clinic: "Congenital Heart Disease in Children."

Dr. Stanley Gibson, Professor of Pediatrics and Chairman of The Department, Northwestern University Medical School, Chicago, Illinois.

9:30 Diagnostic Clinic: "Oral Health in Children."

Dr. John A. Bigler, Associate Professor of Pediatrics, Northwestern University Medical School; Chief of Staff, Children's Memorial Hospital, Chicago, Illinois.

10:00-11:00 *Intermission for Review of Exhibits*

11:00 Diagnostic Clinic: "Lesions of The Sigmoid and Rectum."

Dr. Richard B. Cattell, Surgeon, Lahey Clinic; Surgeon, New England Baptist Hospital; Surgeon-in-Chief, New England Deaconess Hospital, Boston, Massachusetts; President-Elect, Interstate Postgraduate Medical Association of North America.

11:30 Diagnostic Clinic: "Polycythemia Vera; Helpful Concepts in Diagnosis and Treatment."

Dr. Ernest H. Falconer, Clinical Professor of Medicine, University of California Medical School, San Francisco, California.

Noon Intermission

1:30 P.M.

1:30 Diagnostic Clinic: "Lesions of The Adrenal Glands and Pancreas."

Dr. Waltman Walters, Mayo Clinic; Professor of Surgery, University of Minnesota Graduate School of Medicine, Rochester, Minnesota; President, Interstate Postgraduate Medical Association of North America.

2:00 Diagnostic Clinic: "Gastric Vagotomy in The Treatment of Peptic Ulcer."

Dr. Lester R. Dragstedt, Professor and Chairman of the Department of Surgery, University of Chicago School of Medicine, Chicago, Illinois.

2:30 Diagnostic Clinic: "Skin Lesions and Central Nervous System Diseases (Neurocutaneous Disorders)."

Dr. Hans H. F. Reese, Professor of Neuropsychiatry, University of Wisconsin Medical School, Madison, Wisconsin.

3:00-4:00 *Intermission for Review of Exhibits*

4:00 Address: "The Treatment and Prognosis in The Leukemias and Allied Disorders."

Dr. Cyrus C. Sturgis, Professor of Internal Medicine, Director of Simpson Memorial Institute and Chairman of The Department of Internal Medicine, University of Michigan Medical School, Ann Arbor, Michigan.

4:30 Address: "Criteria on Which A Choice Is Made Between Suprapubic, Transurethral and Perineal Methods of Prostatectomy."

Dr. Charles D. Creevy, Assistant Dean and Professor of Urology, University of Minnesota Medical School; Professor of Surgery and Urology, University of Minnesota Graduate School, Minneapolis, Minnesota.

5:00 Address: "Pancreatitis."

Dr. James T. Priestley, Surgical Section, Mayo Clinic; Associate Professor of Surgery, University of Minnesota Graduate School of Medicine, Rochester, Minnesota.

ASSEMBLY DINNER

Grand Ballroom—Hotel Stevens—Informal

7:00 P.M.

For members of the profession, their ladies and friends.

Program

Welcome and presentation of **President Dr. Waltman Walters,** Rochester, Minnesota, by

Dr. Warren H. Cole, President, Chicago Medical Society, Chicago, Illinois; General Chairman, 1950 Chicago Assembly of the Interstate Postgraduate Medical Association of North America.

Addresses

"'I Wish I Knew' or The Analysis of Hobbies Scientific and Otherwise, or Isn't Work Easier."

Dr. Waltman Walters, President, Interstate Postgraduate Medical Association of North America; Mayo Clinic; Professor of Surgery, University of Minnesota Graduate School of Medicine, Rochester, Minnesota.

Presentation of **Dr. Richard B. Cattell,** President-Elect of the Interstate Postgraduate Medical Association of North America; Surgeon, Lahey Clinic; Surgeon, New England Baptist Hospital; Surgeon-in-Chief, New England Deaconess Hospital, Boston, Massachusetts.

FEATS OF MAGIC

Dr. Oliver H. Beahrs

Mayo Clinic, Rochester, Minn.

"VOYAGE TO THREE CONTINENTS"

Color and sound film by

Colonel Robert R. McCormick, Editor and Publisher, The Chicago Tribune, Chicago, Illinois.

Thursday, November 9

8:00 A.M.

8:00 Diagnostic Clinic: "Menopausal Bleeding."

Dr. John I. Brewer, Associate Professor of Gynecol-

ogy, Northwestern University Medical School, Chicago, Illinois.

8:30 Diagnostic Clinic: "The Differential Diagnosis of Jaundice."

Dr. Walter G. Maddock, Professor of Surgery, Northwestern University Medical School, Chicago, Illinois.

9:00 Diagnostic Clinic: "Differential Diagnosis of The Adrenogenital Syndrome, Cushing's Syndrome and the Syndrome of Large, Pale Ovaries."

Dr. Robert B. Greenblatt, Professor of Endocrinology, University of Georgia School of Medicine, Augusta, Georgia.

9:30 Diagnostic Clinic: "The Significance of Frequency of Urination."

Dr. Herman L. Kretschmer, Professor of Urology (Surgery), University of Illinois College of Medicine, Chicago, Illinois; Past President, Interstate Postgraduate Medical Association.

10:00-11:00 *Intermission for Review of Exhibits*

11:00 Diagnostic Clinic: "Treatment of High Diastolic Type of Essential Hypertension by Combined Use of Thiocyanates and Sympathectomy."

Dr. Loyal Davis, Grunow Professor of Surgery and Chairman of the Division of Surgery, Northwestern University Medical School; Attending Surgeon, Passavant Memorial Hospital, Chicago, Illinois.

11:30 Diagnostic Clinic: "Thyroiditis, Simple Goiter and Carcinoma of The Thyroid."

Dr. George Crile, Jr., Cleveland Clinic, Cleveland, Ohio.

Noon Intermission

1:00 P.M.

1:00 Diagnostic Clinic: "Roentgen Evidence of Bronchogenic Carcinoma; A Group of Patients with Atypical and Misleading Clinical Findings."

Dr. Warren W. Furey, Professor of Radiology, Loyola University and Stritch School of Medicine; Chairman of the Executive Committee, Chicago Medical Society, Chicago, Illinois.

1:30 Address: "Coronary Occlusion and Coronary Insufficiency in One Thousand Consecutive Cardiac Consultations."

Dr. Arthur M. Master, Associate Clinical Professor of Medicine, Columbia University College of Physicians and Surgeons, New York, New York.

2:00 Address: "Surgical Management of Obstructing Lesions of The Esophagus."

Dr. Herbert D. Adams, Surgeon, Lahey Clinic and New England Baptist and New England Deaconess Hospitals, Boston, Massachusetts.

2:30-3:00 *Intermission for Review of Exhibits*

(Exhibits will be dismantled at 3:00 P.M.)

3:00 Address: "The Surgical Treatment of Peptic Ulcer."

Dr. I. Ridgeway Trimble, Associate Professor of Surgery, Johns Hopkins University School of Medicine; Associate Professor of Surgery, University of Maryland School of Medicine, Baltimore, Maryland.

3:30 Address: "Third Stage Complications."

Dr. Ralph E. Campbell, Professor of Obstetrics and Gynecology, University of Wisconsin Medical School, Madison, Wisconsin.

4:00 Address: "The Treatment of Arteriosclerotic Popliteal Aneurysms by Simultaneous Lumbar Sympathectomy and Extirpation."

Dr. Collin S. MacCarty, Section on Neurological Surgery, Mayo Clinic; Instructor in Neurosurgery, Mayo Foundation, University of Minnesota.

SPECIAL INFORMATION

PLACE OF ASSEMBLY

The members of the Assembly will have the pleasure of convening in the Hotel Stevens, Chicago. Its equipment is modern in every detail and meets every requirement to carry on the Assembly successfully, such as acoustics, seating capacity, large stage, temporary hospital, electrical equipment, etc.

The opening session of the scientific and clinical program will begin promptly at 8:00 o'clock Monday morning, November 6, 1950.

Registration

The registration fee for the four-day session is $5.00.

Internes, graduate nurses, technicians and dietitians will be admitted upon the payment of $1.00 registration fee. Senior medical students and senior student nurses will be admitted free of charge upon presentation of proper credentials at the registration desk. Undergraduates not admitted.

Guests of the Association (i.e., those appearing on the scientific and clinical program) are requested to register.

Life Members are requested to show their Life Membership card at the time of registration.

Out of town physicians arriving Sunday and Chicago physicians, are urged to register in advance of the opening of the Assembly, Sunday afternoon, November 5, at the Hotel Stevens.

Place of Registration

Everyone attending the Assembly must register. A distinctive badge will be issued to all professional men and women at the time of registration, and a distinctive button will be issued to the senior medical students and senior student nurses. No one will be permitted to attend the scientific and clinical sessions or visit the exhibits unless a badge or button be worn. Your cooperation in this matter is requested.

Technical Exhibits

INTERSTATE POSTGRADUATE MEDICAL ASSOCIATION CHICAGO ASSEMBLY

An important part of every Assembly of the Interstate Postgraduate Medical Association is the Technical Exhibit—a large and attractive display of products and information of value to every member of the medical profession.

Twice daily, there will be special one-hour intermissions in the scientific program of the Chicago Assembly so that all visitors may have ample time to inspect the exhibits and talk with the exhibitors. All of the exhibits will be housed in the Hotel Stevens.

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Consultation Service

This special consultation information service is offered as a regular monthly feature of *Postgraduate Medicine*. Subscribers are invited to call on this Service for answers to difficult medical problems from members of our Editorial Board and our Editorial Consultants best qualified to help. Each question will be answered by mail and those of general interest will be published each month. Address all communications to Consultation Service, *Postgraduate Medicine*, 516 Essex Building, Minneapolis 3, Minnesota.

NONSPECIFIC MYOCARDITIS FOLLOWING INFECTION

QUESTION: Can you give me any information concerning the prognosis and amount of bed rest necessary for patients who have a nonspecific myocarditis diagnosed on electrocardiogram following infection—in this case a kidney infection? The white blood count and sedimentation rate are normal; however, the electrocardiogram remains unchanged.

M.D.—Wisconsin

ANSWER: No specific information can be given in regard to this query. An electrocardiogram cannot be used as a sole criterion for determining the prognosis and amount of bed rest necessary. Every effort must be made to effect a more precise diagnosis. It is not satisfactory to make a simple diagnosis of postinfection myocarditis unless all nutritional factors, adrenal factors and such various unusual conditions as lupus erythematosus, periarteritis and rheumatic fever have been eliminated. If any such condition is present, it should be relieved as nearly as possible, and this, of course, would alter the amount of time the patient is required to remain at bed rest. Naturally the prognosis would depend on the specific diagnosis.

If one is certain that the condition is merely myocarditis following a mild infection and no other factors are involved, then bed rest should not be required any longer than the patient's general physical condition warrants.

TOM D. SPIES

CHONDRODYSTROPHIC DWARFISM

QUESTION: I have a 5-year-old chondrodystrophic dwarf who had the original diagnosis made by x-ray at the age of 2 years. At that time and several other times since the family was told there was nothing to be done. The patient has not improved and she is still only 30 inches in height with the typical clinical findings. Her mentality is good and of course the family is anxious to do something for her.

I have read a few articles that report good results by treating this condition with anterior pituitary extract by mouth. Is this treatment nontoxic? What is the general consensus as to the advisability of trying this form of therapy?

Any information you can give me relative to this condition and the treatment would be appreciated.

M.D.—Texas

ANSWER: There is no known therapeutic regimen which can be recommended for the treatment of chondrodystrophic dwarfism. It is true that C. W. Dunn of Philadelphia has recommended the use of anterior pituitary extract by mouth. However, it is the consensus among endocrinologists that anterior pituitary is of no value when administered orally, and the results shown with this therapeutic agent have not been impressive. More important may be corrective exercise and as little weight bearing as possible in early years, and acceptance of the fact that this form of dwarfism is due to genetic fault and cannot be influenced by hormonal therapy.

ROBERT B. GREENBLATT

TREATMENT OF HYPERHIDROSIS

QUESTION: I am interested in the subject "excessive perspiration" of both hands and feet. Will you please send information that you have available on this condition—etiology and treatment.

M.D.—Philippine Republic

ANSWER: Hyperhidrosis is a constitutional peculiarity with a pronounced emotional background and like so many of the psychosomatic reactions is but little amenable to psychotherapy. Atropine sulfate controls sweating almost everywhere but the palms and soles. Sedatives and antihistaminics have some effect but usually the side effects are disagreeable. In the worst cases sympathectomy has been employed.

Recently the use of diethylaminoethyl xanthene-9-carboxylate methobromide (BANTHINE, Searle) has been successfully used in such cases (J.A.M.A. 143:1331 [August 12] 1950). This is an anticholinergic or parasympatholytic drug. The dose is 50 to 100 mg. every four hours. Side effects are dryness of the mouth, dilatation of the pupils and sometimes constipation. According to the authors the patient may be trusted to adjust the dosage.

WALTER FREEMAN

TREATMENT OF PHLEBOTHROMBOSIS

QUESTION: I have recently had 2 patients who have phlebothrombosis. One is of four years' duration, the other about four months.

Has there been any late or effective therapy devised for the treatment of these cases? If so, please send me information in regard to it.

M.D.—Missouri

ANSWER: So far as I have been able to ascertain there is no very effective treatment for a patient with phlebothrombosis. In phlebothrombosis formation of a thrombus within the vein is not due usually to an inflammatory process. It is probably caused more from stasis of blood, or perhaps other

changes in the blood not due to an inflammatory process. However, the basic cause is not known.

No effective treatment is known other than the use of remedies which are anticoagulants, such as depo-heparin and dicumarol. Sometimes ligation of the peripheral veins has been recommended. Bed rest, elevation of the limb, and local application of heat are the methods which can be easily employed.

JAMES E. PAULLIN

THERAPY FOR PARKINSON'S DISEASE

QUESTION: Please advise me the most acceptable therapy for Parkinson's disease (idiopathic type). Is B_{12} of any value? What is the present status of tolserol for this condition? If it is used, what dosages are recommended and how long may it be continued? Is crude liver of any value?

M.D.—Wisconsin

ANSWER: The existence of so many treatments for Parkinson's disease attests to the fact that there is no particularly outstanding treatment. Every effort, of course, should be made to keep the patient in the best of general health. Vitamin B_{12} and crude liver extract are of no particular value in the treatment of this condition. Atropine, stramonium and hyoscine hydrobromide have been used singly or in combination for many years, with varying results.

In more recent years, extracts of the belladonna root have proved efficacious in certain cases. Panparnit, benadryl, tolserol and artane are newer agents. All have their adherents. It may be wise to try each in turn to determine which drugs give the greatest relief in individual cases. Although adequate rest is indicated, the value of physical medicine and exercises for relief of spasticity must not be forgotten.

TREATMENT OF ACUTE DISSEMINATED LUPUS ERYTHEMATOSUS

QUESTION: I would appreciate any information on the treatment of lupus erythematosus disseminatus. Has ACTH been used in this condition?

M.D.—Virginia

ANSWER: The best treatment for acute disseminated lupus erythematosus is complete bed rest, high caloric diet, and symptomatic therapy. Drugs used in chronic discoid lupus erythematosus, as gold, bismuth, and arsenic, should be avoided. Penicillin in huge doses (5 to 8 million units daily for four or five days) and castration in the young female are occasionally of value.

In the limited number of patients with acute disseminated lupus erythematosus treated with ACTH there has been a dramatic response with almost spectacular disappearance of symptoms of the disease. On withdrawal of the drug there has been almost as dramatic a return of symptoms. This hormone is not curative in acute disseminated lupus erythematosus and is not without danger because of unavoidable serious side reactions.

BEDFORD SHELMIRE

MANAGEMENT OF CASES INVOLVING Rh FACTOR SENSITIZATION

QUESTION: During the next six months I will have four obstetric cases involving Rh factor sensitization and would like to get some reliable late information on the care and treatment of such cases.

The following is the line-up: (1) father and mother Rh negative; expect no trouble; (2) mother Rh negative; first baby o. k.; second baby, fourth month miscarriage; (3) mother Rh negative; first baby died three days before delivery; second baby full term saved by transfusion; (4) mother Rh negative; first baby o. k.; second baby, three month miscarriage; third baby, three month miscarriage.

I would like some reliable information on the care and treatment of such cases. There is much literature on the subject but it is hard to evaluate and select the reliable information. If you can assist me I will appreciate any information you can give me or advise me where I can get it.

M.D.—Nebraska

ANSWER: With regard to the cases mentioned in the letter:

1. When both the expectant mother and father are Rh negative, all the children will be Rh negative, so there is no danger from Rh sensitization.

2. Rh sensitization does not cause miscarriages.

3. Rh sensitization rarely affects the first born baby unless the mother has been previously sensitized by a blood transfusion or blood injection.

4. Rh sensitization does not cause miscarriages.

The letter sent by the correspondent makes no mention of tests for Rh antibodies. A diagnosis of erythroblastosis cannot be made readily without such tests. The mere fact that the mother is Rh negative is only feeble circumstantial evidence, and is not diagnostic.

The confusion in the literature is due to the fact that the serologic tests especially for Rh antibodies are delicate, so that errors are common. Unfortunately, many of the reports in the literature are based on such faulty observations. While the subject is complex, and there are many things which are difficult to explain, the observations which are most difficult to account for are those which are incorrect.

REFERENCES

1. Wiener, A. S.: Treatment of erythroblastosis fetalis by exchange transfusion. Postgrad. Med. 7:1 (January) 1950.
2. Wiener, A. S., Wexler, I. B., and Hurst, I. G.: The use of exchange transfusion for the treatment of severe erythroblastosis due to A-B sensitization, with observations on the pathogenesis of the disease. Blood 4, No. 9 (September) 1949.
3. Wiener, A. S., and Wexler, I. B.: Results of therapy of erythroblastosis with exchange transfusion. Blood 4, No. 1 (January) 1949.
4. Pickles, M. M.: Haemolytic Disease of the Newborn. Springfield, Illinois, Charles C Thomas, 1949.

ALEXANDER S. WIENER

New Drugs *and* Instruments

Information published in this department has been supplied by the manufacturers of the products described.

CEBETINIC* TABLETS

PURPOSE: Hematinic.

COMPOSITION: Each yellow, pumpkin-seed shaped tablet contains:

Ferrous gluconate	5.0 gr.
Vitamin B_{12}	1.0 microgram
Folic acid	0.67 mg.
Thiamine hydrochloride (B_1)	2.0 mg.
Riboflavin (B_2, G)	2.0 mg.
Pyridoxine hydrochloride	0.5 mg.
Nicotinamide	10.0 mg.
Ascorbic acid	25.0 mg.

INDICATIONS FOR USE: Prevention and treatment of iron-deficiency anemia; in anemias of pregnancy, growing children, and persons suffering from conditions resulting in chronic loss of blood or faulty absorption caused by disorders of the alimentary tract.

DOSAGE AND ADMINISTRATION: Adults, 3 or more tablets daily; children, 1 to 3 tablets daily.

HOW SUPPLIED: Bottles of 60 and 500 tablets.

PRODUCER: The Upjohn Co., Kalamazoo, Mich.

*Trademark.

AUREOMYCIN CRYSTALLINE

PURPOSE: Recrystallized form of Aureomycin.

DESCRIPTION: Said to be nearly free of trace elements which in the past were believed to cause gastrointestinal reactions.

HOW SUPPLIED: All Aureomycin products will henceforth be produced with the new Aureomycin Crystalline.

PRODUCER: Lederle Laboratories Division, American Cyanamid Co., Pearl River, New York.

KONDRETABS

PURPOSE: Bulk laxative tablet for control of constipation.

COMPOSITION: Each tablet contains:

Irish moss concentrate ..... 0.25 gm. (3.8 gr.) equivalent to 0.625 gm. (10 gr.) of Irish moss and methyl cellulose 0.5 gm. (7.7 gr.).

DOSAGE AND ADMINISTRATION: 1 or 2 tablets 3 times a day, with a full glass of water.

HOW SUPPLIED: Bottles of 50 and 100 tablets.

PRODUCER: The E. L. Patch Company, Stoneham, Mass.

LITRISON CAPSULES

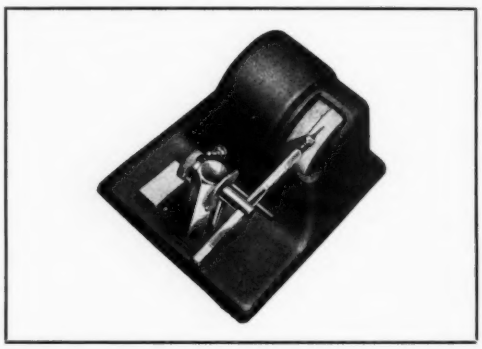
PURPOSE: Dietary supplement in management of liver diseases.

COMPOSITION: Contain lipotropic agents, vitamin B_{12}, folic acid, vitamins A and D, and B complex factors.

INDICATIONS FOR USE: Cases of reparable damage or functional impairment of the liver responsive to lipotropic factors and fat and water-soluble vitamins.

DOSAGE AND ADMINISTRATION: A daily dose of 6 capsules is recommended.

PRODUCER: Hoffmann-La Roche, Inc., Nutley, N. J.



GUILD POINTER

PURPOSE: Hypodermic needle grinder.

DESCRIPTION: Needle holding bar can be set for long, medium, or short bevels. Put the needle on the holder, set the bevel, turn the switch. Touch the needle to the stones and the finished needle point is razor-sharp and smooth. Unit finished in gray baked enamel with all bare metal parts in heavy chromium plate.

PRODUCER: Guild Instrument Company, Cincinnati, Ohio.

DUCOBEE

PURPOSE: Aqueous solution of vitamin B_{12} for intramuscular injection.

COMPOSITION: Each 1-cc. ampule contains 15 micrograms of crystalline vitamin B_{12}.

INDICATIONS FOR USE: Pernicious anemia, nutritional macrocytic anemias and sprue. Useful in patients hypersensitive to liver or liver extracts.

HOW SUPPLIED: In 1-cc. ampules, boxes of 6 and 25.

PRODUCER: George A. Breon & Co., Kansas City, Mo.

CEHISTRA TABLETS

PURPOSE: Treatment of allergic disturbances responding to antihistamine or to high-dosage vitamin C therapy.

COMPOSITION: Each tablet contains:

Prophenpyridamine (available as the maleate)	10 mg.
Ascorbic acid	100 mg.
Aspirin	320 mg.

in an alkalizing base consisting of sodium bicarbonate (1820 mg.), calcium hydroxide, and citric acid.

DESCRIPTION: Effervescent tablets dissolve in water to form an orange-flavored solution.

DOSAGE AND ADMINISTRATION: Average dosage is 1 tablet every 3 or 4 hours, not to exceed 8 tablets per day.

HOW SUPPLIED: Vials of 10 tablets.

PRODUCER: Organon, Inc., Orange, N. J.

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